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S. M. S. Medical Library

RIGHT AND WRONG USE OF DIURETICS.....	PAGE 1639
Clinic of Dr. Francis W. Peabody, <i>Peter Bent Brigham Hospital</i>	
THE VITAL CAPACITY OF THE LUNGS IN HEART DISEASE.....	1655
Clinic of Dr. I. Chandler Walker, <i>Peter Bent Brigham Hospital</i>	
THE CAUSES AND TREATMENT OF SEASONAL HAY-FEVER.....	1673
Contribution by Dr. Charles W. McClure, <i>Peter Bent Brigham Hospital</i>	
TREATMENT OF FUNCTIONAL GASTRO-INTESTINAL DISTURBANCES.....	1693
Clinic of Dr. Samuel A. Levine, <i>Peter Bent Brigham Hospital</i>	
RAPID HEART ACTION.....	1707
Clinic of Dr. Elliott P. Joslin, <i>New England Deaconess Hospital</i>	
PRACTICAL LESSONS FOR PHYSICIANS AND PATIENTS IN DIABETES.....	1723
Clinic of Dr. George R. Minot, <i>Massachusetts General Hospital</i>	
TWO CURABLE CASES OF ANEMIA.....	1733
Clinic of Dr. Francis M. Rackemann, <i>Massachusetts General Hospital</i>	
THE VACCINE TREATMENT OF ASTHMA.....	1751
Clinic of Dr. James P. O'Hare, <i>Peter Bent Brigham Hospital</i>	
A CASE OF VASCULAR HYPERTENSION WITH ANGINA PECTORIS AND CEREBRAL HEMORRHAGE. AUTOPSY.....	1767
Clinic of Dr. Edwin A. Locke, <i>Boston City Hospital</i>	
SYPHILIS OF THE LUNGS.....	1785
Contribution by Dr. Frederick T. Lord, <i>Massachusetts General Hospital</i>	
A DISCUSSION OF THE DIFFERENTIAL DIAGNOSIS OF A CASE OF SPINAL TUMOR.....	1799
Clinic of Dr. William H. Robey, <i>Boston City Hospital</i>	
MALIGNANT DISEASE OF THE LUNGS.....	1811
Clinic of Drs. Paul D. White and C. Sidney Burwell, <i>Massachusetts General Hospital</i>	
THE CLINICAL SIGNIFICANCE OF CHANGES IN THE FORM OF THE ELECTROCARDIOGRAM..	1839
Clinic of Dr. Stanley Cobb, <i>Massachusetts General Hospital</i>	
SOME NEUROLOGIC ASPECTS OF CHOREA.....	1863
Clinic of Dr. Roger I. Lee, <i>Massachusetts General Hospital</i>	
SUBDIAPHRAGMATIC INFLAMMATORY CONDITIONS.....	1871
Contribution by Drs. Francis W. Palfrey and S. Burt Wolbach, <i>Harvard University Medical School</i>	
TYPHUS FEVER.....	1877
Contribution by Dr. Horace Gray, <i>New England Deaconess Hospital</i>	
SIZE AND WEIGHT IN 130 BOARDING-SCHOOL BOYS (MIDDLESEX).....	1899
 Index to Volume 4.....	 1915

THE MEDICAL CLINICS OF NORTH AMERICA

VOLUME 4

NUMBER 6

CLINIC OF DR. HENRY A. CHRISTIAN

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RIGHT AND WRONG USES OF DIURETICS¹

GENTLEMEN: Today I am going to discuss the use of diuretics and, prefatory to that, summarize very briefly renal function. The kidney is an excretory organ through which various substances leave the body. Except for very small quantities of hippuric acid the human kidney is almost purely an instrument of excretion, and it is the influence of drugs on the kidney in relation to excretion that concerns us in therapeutics. Drugs that increase renal activity are diuretics. They may accomplish this increased renal activity in various ways.

Without going into the details of the pharmacologic action of the drugs used as diuretics and without undertaking to discuss their action in an exhaustive way, a brief résumé of the present conception of renal activity in relation to the action of diuretics is needed for a general understanding of the subject in its clinical bearings.

The kidney has a very rich vascular supply. The blood from the general circulation reaches the glomerulus, where it flows into a capillary system. It is then gathered into a small efferent artery, which soon again breaks up into a capillary system about the renal tubules. Finally, the blood is gathered into an efferent venous system. This mechanism of circulation affords two places where the blood with a slow current in thin-

¹From the Medical Clinic of the Peter Bent Brigham Hospital, Boston, Mass.

walled capillaries can exchange materials in solution in it with the contents of the tubules. According to the modern theory (Cuslly), from the glomerular capillary area substances pass through the glomerular membrane by filtration, while by means of reabsorption through epithelial cells into the peritubular capillary system part of this material passes back into the circulation. The composition of the urine in last analysis depends on the balance between glomerular filtration and tubular reabsorption in relation to the composition of the blood.

The amount and quality of urine excreted theoretically can be influenced by changing the composition of the blood, the rate and pressure of blood flow, the character of the filtration and absorption membranes, or the cellular activity of the epithelial cells. Some urinary constituents, such as urea, called non-threshold substances, after passing through the glomerular membrane by filtration, undergo no reabsorption in the tubules; others, known as threshold substances, are reabsorbed in varying degree by the tubular epithelium; some, as glucose, practically completely; others, like sodium chlorid, only partially. The latter only appear in the urine when they exceed a certain amount in the blood, *i. e.*, exceed their so-called threshold value. This is a very complex mechanism not as yet thoroughly understood for the normal kidney. Both cellular vital activity (physiology) and the physical properties of living membranes and of dissolved substances (physical chemistry) play their part in it. Diuretic drugs, to produce their effects, must influence this complex mechanism (pharmacology), and, furthermore, not alone in the normal kidney, but under changed conditions brought about in its structure by disease (pathology); changes which may be focal or diffuse and involve various levels and structures of the renal excretory unit, *i. e.*, the glomerulus and its tubules.

If a diuretic is effective, it either increases the amount of water or solids of the urine; usually both are effected, but in a varying ratio. As rational therapeutists we should use diuretics only when conditions indicate the desirability of accomplishing this end, and we should be guided in the continuance of their use by observations as to the results produced. In other words,

having given a patient a diuretic, we must determine whether a diuresis is produced as the first step in estimating the efficacy of our treatment. The simplest observations to make are to measure the amount of urine in relation to the fluid intake and to determine its specific gravity. In addition, we can quantitate certain constituents of the urine in relation to food and fluid intake to see whether they are being excreted in increased amount as an effect of the treatment instituted, and we can measure renal function by various means to see whether it is being improved or not. Finally, in case of hypothetical toxic substances we can only form an estimate of their excretion by noting a change in symptoms.

As already indicated, the renal mechanism is complex and diuretics can influence it in various ways. To a certain extent the pharmacologist has given us information as to how certain substances produce a diuretic effect, and it is quite certain that all do not work in the same way. When it comes to the diseased kidney we have but little information as to the detailed mechanism of different diuretic substances (pathologic physiology and pathologic pharmacology); what we know is based largely on clinical observation, and this has shown that different diuretics have different actions, at least one is sometimes effective when another given under the same conditions, as far as we can tell, is ineffective.

In practical therapeutics what do we aim to accomplish by using diuretics? We seek to remove excess water, thereby decreasing edema, and to remove deleterious substances which have accumulated in the body. These deleterious substances are nitrogenous compounds, sodium chlorid, possibly other inorganic substances, and that hypothetical toxic substance that causes the manifestations we know as uremia. To use diuretics with this intent is rational, and it is a right use for a diuretic if we have evidence that it is accomplishing the desired end. If we have no evidence, as we observe the case, that a diuresis in this sense is taking place, we are not justified in continuing the diuretic, for we have no evidence that our therapeutics is doing the patient any good. Furthermore, we have evidence that a

diuretic producing no diuresis increases renal fatigue or renal irritation, or both, and actually does damage to the renal structures and decreases such excretion as otherwise would take place. When this is the result it is wrong to continue the use of a diuretic.

As a general rule, an increase in any urinary constituent following diuretic drugs is accompanied by an increased output of water if there is an available source of water either in tissue fluid (edema) or in fluid intake. There are occasional exceptions to this, but they are few enough for water output to be a very satisfactory index of a diuresis, and when there is no water increase it is rare for there to be any considerable increase in the other urinary constituents. Weighing the patient and measuring the urine amount in relation to fluid intake become the best and at the same time are the simplest means of determining a diuresis. Consequently, both observations should be made regularly as a means of determining effectiveness of a diuretic, and if these observations are not being made when giving a diuretic we fail in acting as rational therapists.

When water is excreted by the kidney in increased amount, with few exceptions, it carries out an increased amount of other urinary constituents and often increases urine output out of proportion to the added fluid intake, and in this sense water is a diuretic. Figure 188 illustrates this. Here in a patient with chronic nephritis, showing a considerable edema of about four months' duration, and without any evidence of cardiac insufficiency, an increased intake of fluid produced a slight diuresis. A few days later theobromin sodiosalicylate failed to cause adiuresis, and subsequently potassium acetate was ineffectual. Moreover, like other diuretics, water increases renal work and may lead to renal fatigue and decreased renal output when given to an individual or animal with a damaged or diseased kidney. Consequently, fluids should be looked upon in a therapeutic sense as one of the diuretic group.

The symptom which occurs most commonly as an indication for using a diuretic is the presence of edema. If edema, as very often is the case, is moderate in amount, it is not an in-

dication for using a diuretic. When it causes annoyance we should seek to remove it by a diuretic along with other appropriate measures. As with edema there is already an excess of fluid beyond the ability of the kidney and other water-excreting viscera to eliminate, water is not a proper diuretic substance for these patients. Caffein, theobromin sodiosalicylate, and theophyllin are proper diuretics to remove edema, and one or the other should be used under these conditions. They should be continued to be used, however, only if they increase the amount

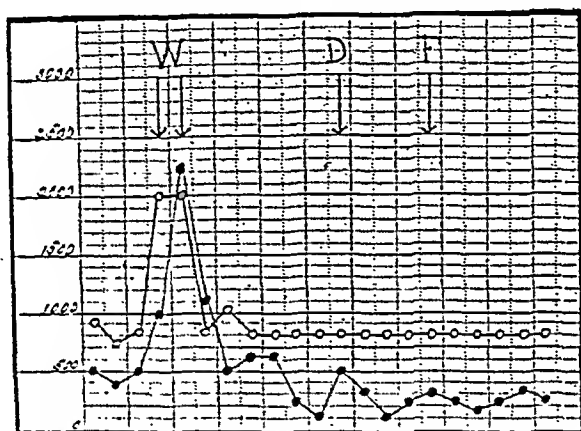
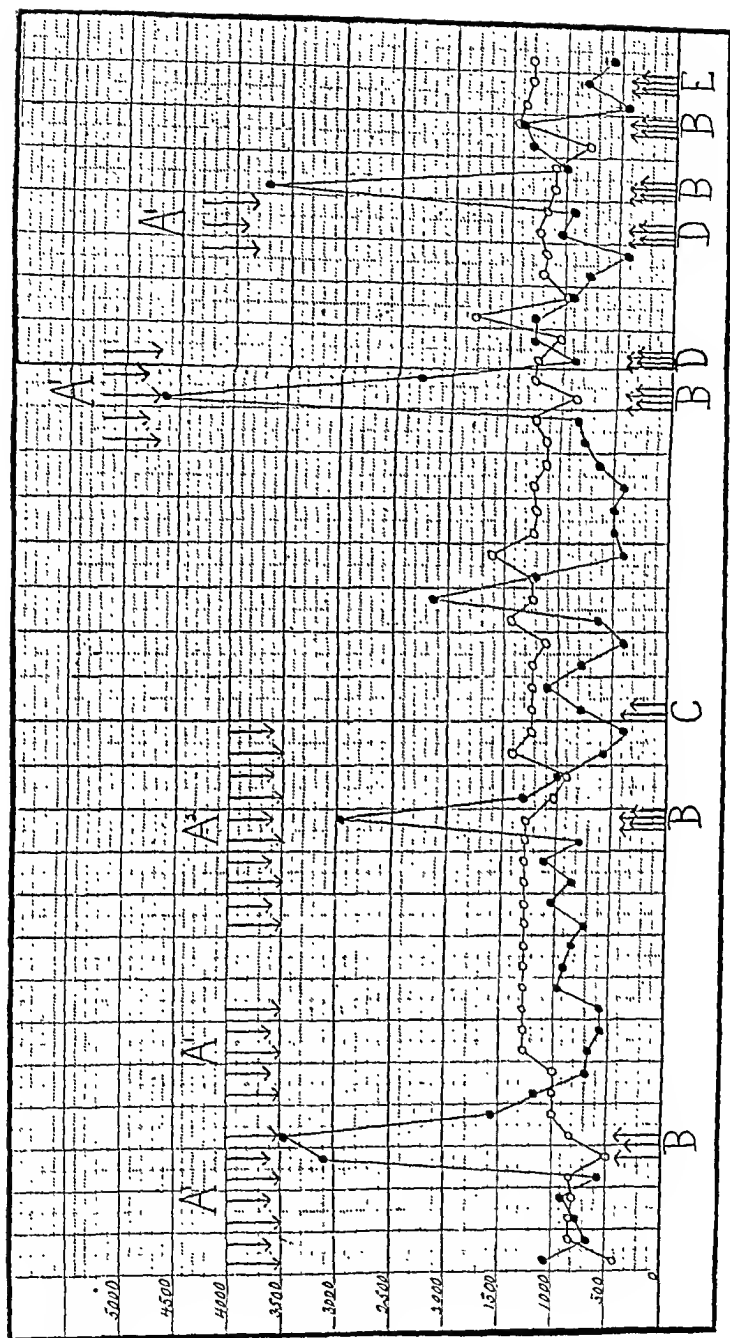


Fig. 188.—The solid black dots indicate the twenty-four-hour amount of urine in cubic centimeters. The black circles indicate the twenty-four-hour amount of fluid intake in cubic centimeters. Each arrow under W indicates a day on which the patient received an additional 1000 c.c. of water; the arrow under D indicates a day on which the patient received three doses of 0.5 gm. each of theobromin sodiosalicylate, and the arrow under F a day on which the patient received two doses of 1 gm. each of potassium acetate.

of urine. Failing to obtain a diuresis from one, another should be tried, since as the result of conditions which we cannot predict or predetermine sometimes one of this group is efficient when another is not. Usually it is best to change the diuretic rather than increase the dose if an average dose is being given. This is well illustrated in Figs. 189, 190. Here in a patient with aortic stenosis and insufficiency, and edema of essentially cardiac



origin, diuresis is produced by theophyllin and by caffein sodio-benzoate in combination with digitalis, as shown in Fig. 189, while there is absence of diuresis from theobromin sodiosalicylate. You will note toward the end of the chart that the failure of a diuresis from theobromin occurs when diuresis is possible, because following a failure to secure diuresis from theobromin it was produced by theophyllin.. In order to determine whether this difference was due to a lack of absorption of the theobromin the experiment was repeated with intravenous dosage; as shown in Fig. 190 theophyllin produced a marked diuresis and theobromin no diuresis.

It should be remembered always that diuretics increase renal work, tend to produce fatigue, with a consequent reduction in activity of renal function, and may easily do harm. So if diuresis does not ensue, one should be very cautious in continuing their use or in increasing the dosage. Moreover, when a diuresis occurs, renal fatigue follows, and a period of rest is desirable. Hence, intermittent rather than continuous usage of diuretics is indicated, one day giving the drug and the next day omitting it.

When circulation is efficient and edema has arisen from inability of the kidney to excrete water, in other words, with a renal edema, it is rare for a diuresis to follow the use of any of this group of diuretics, whatever the dosage or the means of giving the diuretic, by mouth, subcutaneously, or intravenously. It is in this group that diuretics are often used to the damage of the patient, and when pushed may greatly depress renal function. This failure to get a diuresis is well shown in the following figures. Figure 191 shows a failure of diuresis twice from single doses of

Fig. 189.—The solid black dots indicate the twenty-four-hour amount of urine in cubic centimeters. The black circles indicate the twenty-four-hour amount of fluid intake in cubic centimeters. Each arrow under A¹ indicates a day on which the patient received three doses of 10 c.c. each of an infusion of digitalis. Each arrow under A² indicates a day on which the patient received two doses of 10 c.c. each of an infusion of digitalis. Each arrow over B indicates one dose of 0.5 gm. of theophyllin. Each arrow over C indicates one dose of 0.2 gm. of caffein sodio-benzoate. Each arrow over D indicates one dose of 0.3 gm. of theobromin sodiosalicylate. Each arrow over E indicates one dose of 0.5 gm. of theocin sodioacetate.

0.3 gm. of theophyllin, whether given with or without an accompanying course of digitalis, to a patient who gave the following history: A man aged thirty-eight noticed, eleven days before

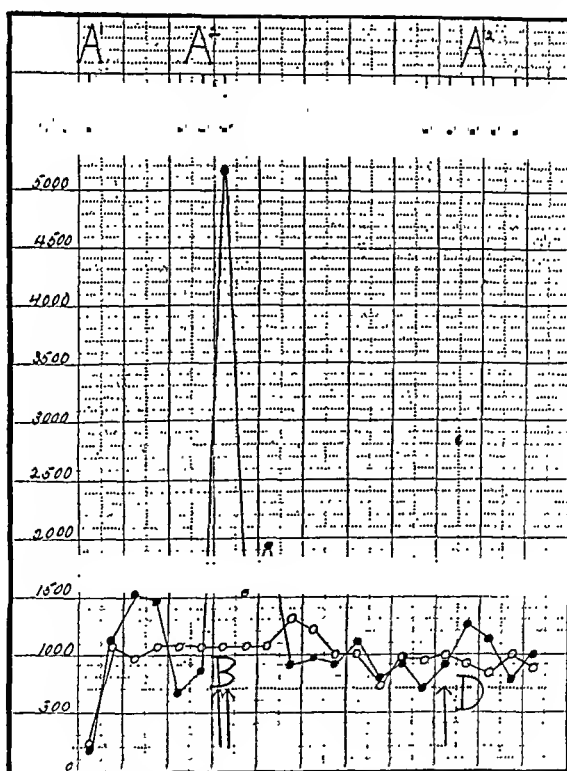


Fig. 190.—The solid black dots indicate the twenty-four-hour amount of urine in cubic centimeters. The black circles indicate the twenty-four-hour amount of fluid intake in cubic centimeters. The arrow under A¹ indicates a subcutaneous dose of 1 c.c. of digipuratum and under A² a day on which the patient received three doses of 10 c.c. each of an infusion of digitalis. The arrows at B indicate two doses of 0.5 gm. each of theophyllin given intravenously and at D a dose of 1 gm. of theobromin sodiosalicylate given intravenously.

coming into the hospital, that his legs began to swell. Five days before he came in he found that his face was swollen. Two days before admission edema had involved his genitalia.

This patient had a normal blood-pressure, signs of fluid in his thorax, possibly some fluid in his abdomen, and a marked degree of subcutaneous edema. On admission his urine contained a large amount of albumin, many hyaline and granular casts, many of which had fat attached, and a very few red blood-cells. His excretion of phenolsulphonphthalein was 28 per cent. in two hours. His non-protein nitrogen was 36 mgm. per 100 c.c. of blood. You will also see in this chart that digitalis by itself produced no diuresis.

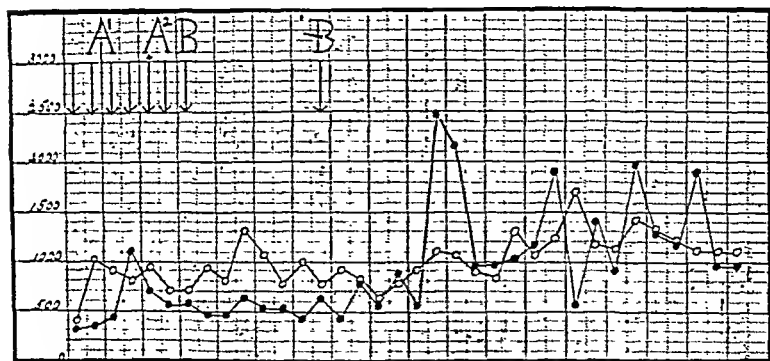


Fig. 191.—The solid black dots indicate the twenty-four-hour amount of urine in cubic centimeters. The black circles indicate the twenty-four-hour amount of fluid intake in cubic centimeters. Each arrow under A¹ indicates a day on which the patient received three doses of 0.1 gm. each of powdered digitalis leaves; under A² a day on which the patient received two doses of 0.05 gm. each of powdered digitalis leaves. Each arrow under B indicates a dose of 0.3 gm. of theophyllin.

In another patient no diuresis followed theobromin, theophyllin, urea, or sodium chlorid, as shown in Fig. 192, which is from a patient who gave the following history: A man of thirty-one developed swelling in his legs three and a half months before he came into the hospital. On admission he showed considerable edema of his legs and trunk, and definite signs of fluid in his abdomen. His phenolsulphonphthalein excretion varied between 28 and 52 per cent. in two hours. His non-protein nitrogen was 23 mgm. per 100 c.c. of blood. His urine

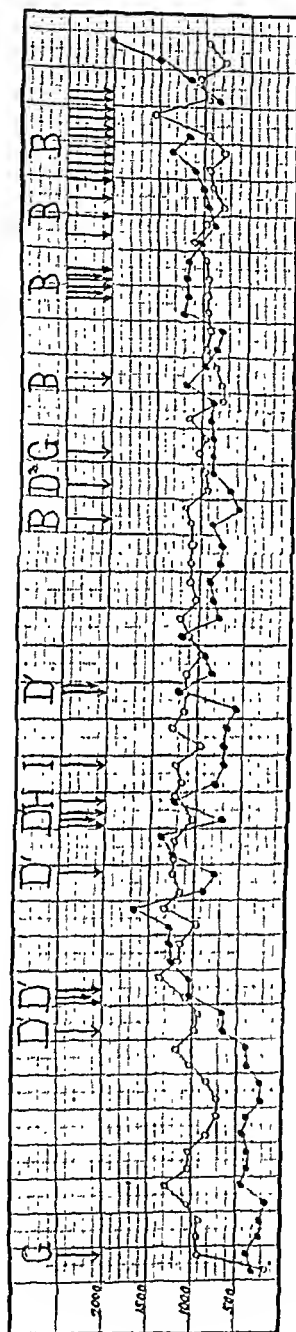


Fig. 192.—The solid black dots indicate the twenty-four-hour amount of urine in cubic centimeters. The black circles indicate the twenty-four-hour amount of fluid intake in cubic centimeters. Each arrow under B indicates a dose of 0.3 gm. of theophyllin; under D¹ a dose of 0.25 gm. of theobromin sodiosalicylate; under D² a dose of 0.5 gm. of theobromin sodiosalicylate; under G moving 2650 c.c. of ascitic fluid; under H, 20 gm. of urea, and under I, 10 gm. of sodium chlorid.

picture was essentially the same as in the preceding patient. His blood-pressure was 150 mm. of mercury. In still another patient

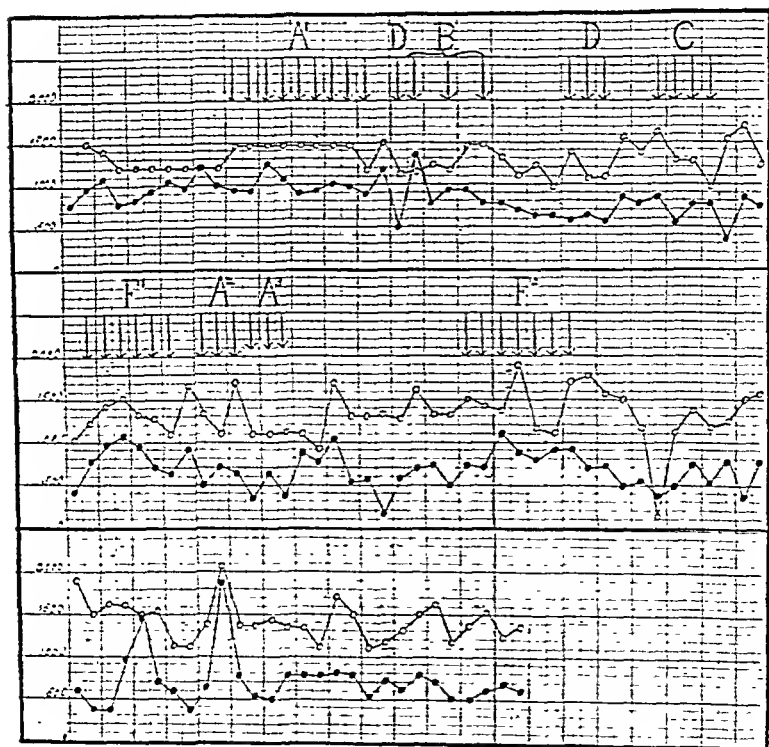


Fig. 193.—The solid black dots indicate the twenty-four-hour amount of urine in cubic centimeters. The black circles indicate the twenty-four-hour amount of fluid intake in cubic centimeters. Each arrow under A^1 indicates a day on which the patient received three doses of 0.1 gm. each of powdered digitalis leaves; under A^2 a day on which the patient received two doses of the same, and under A^3 a day on which the patient received two doses of 0.05 gm. each of powdered digitalis leaves. Each arrow under B indicates a dose of 0.5 gm. of theophyllin; under C a day on which the patient received 0.13 gm. of caffeine citrate every four hours; under D a dose of 0.5 gm. of theobromin sodiosalicylate; under F^1 a dose of 1 gm. of potassium citrate, and under F^2 a day on which the patient received two doses of 0.5 gm. each of potassium citrate.

of very similar type digitalis, theobromin, theophyllin, caffeine, and potassium citrate yielded no diuresis, as is shown in Fig. 193.

On the other hand, when there is edema because circulation is

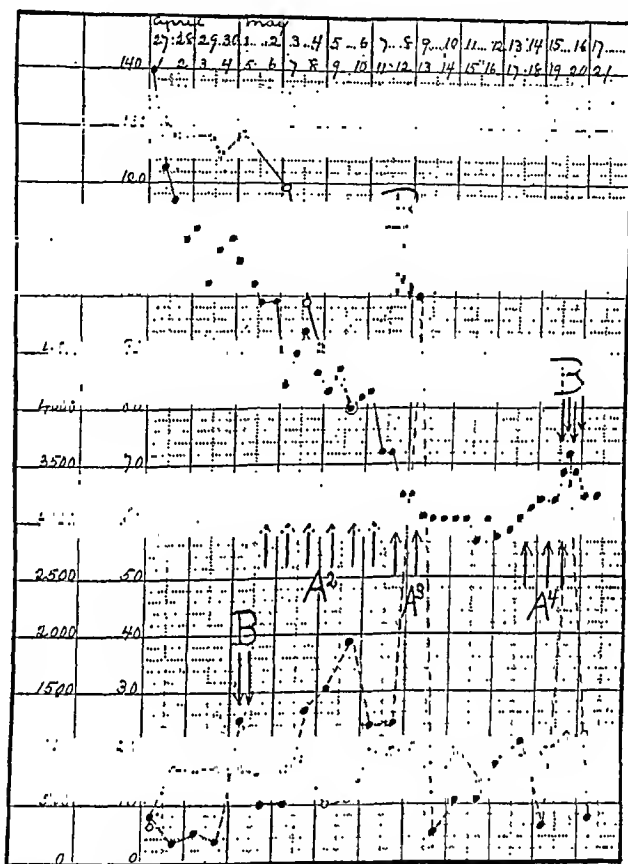


Fig. 194.—The solid black dots connected by a solid line indicate radial pulse rate; the circles connected by a solid line indicate apex heart rate. The circles connected by a broken line indicate fluid intake; the solid dots connected by a broken line indicate urine output. Each arrow under B represents 0.3 gm. of theophyllin; those over A represent digitalis; each arrow over A² representing a day on which patient received three doses of 0.1 gm. of powdered leaves, each over A³ two doses of 0.05 gm., and each over A⁴ three doses of 10 c.c. of infusion.

inefficient and renal cells are little damaged, these diuretics, especially when combined with digitalis, produce a marked

increase in urine flow and act to reduce rapidly the edema. This group of diuretics are indicated for this type of case and produce best effects when given in moderate dosage and intermittently.

With edema of renal origin digitalis does not act to increase urine output unless there is some cardiac incompetence (Figs. 191, 193). If, however, edema is of cardiac origin, digitalis by itself produces a diuresis, and in this sense and for these cases is a diuretic drug. In this group of cases of edema of cardiac origin digitalis and the other diuretic drugs combine to produce a more marked diuresis than if used alone, and it is advisable to use them in combination (Figs. 189, 190, 194). They should not, however, be combined in one prescription, as is frequently done, because digitalis ought to be given continuously until a digitalis effect is produced, and then the dosage should be decreased so as to just maintain the action, while the diuretic drugs should be given intermittently in moderate dosage, and stopped when there is evidence of renal fatigue. Obviously, these requirements of effective therapeutics cannot be met when both drugs are combined in one mixture and the amount given of the one cannot be changed without a corresponding change in the other.

The next symptom, of importance rather from its seriousness than from its frequency, which calls for a diuresis, is uremia. Water is the most effective diuretic for uremia. Our aim is to eliminate from the circulating blood a hypothetical toxic substance. If water increases urine flow, there is more chance of the toxic substance being excreted. If the water fails to increase urine flow, it will lead to edema, and apparently remove toxic substances from the blood to the interstices of the connective tissue, where they do little harm. At least it is a matter of clinical record that an increasing edema sometimes is accompanied by a decrease in toxic symptoms, and vice versa. Water may be given by mouth as an increased fluid intake, or as normal saline solution by rectal seepage, by subcutaneous infusion, or by intravenous injections. It seems most effective when it can be given via the gastro-intestinal route.

With the water in uremia diuretic drugs may be used, but a

uremia occurs with a seriously damaged kidney it is not likely that the diuretic drug will increase the urine flow. As they may act to decrease renal activity, caution must be used in giving them so that the effect of the water is not minimized. In the case of uremia we have no means of determining the effects of our therapy other than by the effect on symptoms. There is no substance which we can quantitate in the urine to measure whether or not the cause of the uremic symptoms is being eliminated from the body.

Another injurious substance we seek to remove from the body is sodium chlorid. Sodium chlorid retention is often associated with marked edema, and so water is of little use in its removal. There is, however, a form of dry salt retention in which possibly salt retention does harm. Recently it has been claimed that salt retention is an important factor in causing high blood-pressure, and in these cases there is no edema. In such cases it seems rational to think that various diuretics would increase salt output, but there seem to be few observations on record of the action of diuretics under these circumstances. Water, caffein, theobromin sodiosalicylate, and theophyllin, however, should have a trial in these cases of dry salt retention. Of them, water in large amount theoretically might be considered least likely of producing an improvement in hypertensive cases because of its likelihood of increasing the blood-pressure and indirectly decreasing renal function thereby. In other words, under these circumstances water is not likely to increase salt elimination and serve as a satisfactory diuretic.

In sodium chlorid retention with edema diuretics very rarely cause a diuresis (Figs. 191-193), and so very rarely increase salt and water elimination. A decreased salt intake may allow of an output of retained salt if the intake is reduced below output. In many cases the salt and water retention is very slowly overcome, and satisfactory progress is not made unless other methods of fluid elimination are used. In such cases a tentative use of caffein, theobromin, and theophyllin should be made. In my experience they but rarely produce a diuresis in this group of cases, and so are ineffectual. If on trial

this proves to be the case, they should have no further use in this type of patient.

The nitrogenous substances are the last of the injurious retention products to be considered. Here, as a rule, we are dealing with a severely injured kidney, and diuretics are ineffective, with the possible exception of water. It may be that the nitrogenous substances in the amounts retained are not in themselves toxic, but merely are an index of the very bad renal function, while the symptoms that go with their retention result from the retention of unknown substances. They serve, however, as an indication for obtaining a better renal function if it can be obtained in any way. Here, as with all renal disturbances, diuretic drugs are but one means of increasing body elimination. In discussing diuretics I have made no mention of other channels of elimination. I have assumed, however, that these other means will be utilized in combination with diuretics as the conditions in each case indicate.

Finally, diuretic drugs should never be used because of a diagnosis of renal lesion; they have definite indications for their use and should be used only when these indications are met with. Used judiciously under proper conditions they are productive of good. Wrongly used they do harm. There is a right use and a wrong use for all diuretics. I have confined my attention to a few which are generally used. Further study of the problem should throw more light on these, and better ones very surely can be found. The action of diuretics on the damaged rather than on the normal kidney is what particularly needs further investigation from pharmacologists and clinicians.



CLINIC OF DR. FRANCIS W. PEABODY

PETER BENT BRIGHAM HOSPITAL

THE VITAL CAPACITY OF THE LUNGS IN HEART DISEASE¹

THE cases which are about to be demonstrated are patients with heart disease, and the discussion of them will be limited largely to the question of dyspnea. Although shortness of breath is only one of the many symptoms of heart disease, it seems justifiable to devote considerable attention to an analysis of it because dyspnea is by far the most common, as well as one of the earliest, symptoms produced by cardiac weakness. In occasional cases palpitation and precordial pain may be the earliest presenting symptoms, but there is usually associated with them a tendency to dyspnea on exertion, which may, however, be completely masked by the more acutely distressing subjective symptoms. Such evidences of cardiac failure as cyanosis, edema of the legs, and hepatic tenderness are late signs of cardiac weakness, and when they are present an abnormal tendency to dyspnea is rarely absent. Many patients with heart disease, it is true, do not complain of shortness of breath. This is especially noticeable in young persons in the early stages of valvular heart disease which is the result of rheumatism or some other acute infection. In such cases the injury has been largely limited to the heart valves and the damage to the heart muscle has been comparatively slight. The strong, healthy myocardium is still able to compensate for the lesion of the valves, so that the functional efficiency of the heart remains normal. Striking instances of this were seen during the war, when it was frequently

¹From the Medical Clinic of the Peter Bent Brigham Hospital, Boston, Mass.

observed that soldiers with definite disease of the aortic and mitral valves were able to carry on full duty without limitation of their activities. In such men heart disease was in the nature of an accidental finding, for there was apparently no decrease in the reserve power of the heart. For practical purposes such hearts are essentially efficient, for they are capable of maintaining a circulation which meets all the demands made upon it when the skeletal muscular system is working at its utmost. These are instances of cardiac disease with complete compensation and must be classed as belonging to the heart disease of "signs," in contrast to the heart disease of "symptoms." Later in the course of such cases, either as the result of subsequent acute infections, of vascular changes, or of a further development of the inflammatory process, the heart muscle becomes less efficient and its normal reserve power is reduced. At first the heart is unable to adapt the circulation to the needs of the body when the demands on it are great, as in severe exercise, but later the weakness of the heart becomes so pronounced that the circulation is insufficiently maintained even when the body is at complete rest. In either case dyspnea usually forms an important part of the clinical picture, occurring, on the one hand, only on exertion and, on the other hand, even when the patient is at complete rest. In sharp contrast to the clinical picture of these cases of heart disease, which begin with physical signs and only develop symptoms when the course is advanced, are those which are characterized from the beginning by the symptoms of cardiac weakness. These are the cases of heart disease which are particularly common after middle age and in which the pathologic lesion is usually limited to the myocardium. Attention is usually called to these cases by the appearance of symptoms referable to the heart, and of these symptoms dyspnea on exertion is by far the most common. Dyspnea may be extremely distressing at a time when the physical examination of the heart by all modern methods, including x-ray and electrocardiograph, shows very little that is abnormal. Precordial pain and palpitation may also be early symptoms, but in most cases the tendency to dyspnea will be present, although it may not be prominent in

the patient's mind because he has limited his physical exertion so completely, in order to avoid pain, that he has had no opportunity of testing his tendency to dyspnea. Dyspnea, therefore, is to be regarded not merely as a general symptom of heart disease, but as important evidence of a decreased functional efficiency of the myocardium. The tendency to dyspnea is a good index of what is known as "the reserve power of the heart." Under normal circumstances the reserve power of the heart is very great, and the normal heart muscle can usually adapt the circulation of the blood to meet the demands made on it by the greatest amount of physical exercise that the subject is capable of carrying on. As the heart muscle becomes weak this reserve power is cut down and a much smaller amount of physical exertion produces dyspnea. We know from clinical experience that a patient with heart disease is not doing well when he tells us that he gets short of breath more easily than formerly. When, on the other hand, he tells us that he can go up two flights of stairs without getting out of breath, whereas he formerly could go up only one flight, we know that his cardiac condition is improving. Such statements as to the variation in the tendency to dyspnea give us only a general, rather vague idea of the patient's condition, and they are so often colored by his subjective state of mind that they lack the value of precise quantitative observations. Nevertheless, the degree of dyspnea or the tendency to dyspnea is very generally used as an index of the cardiac condition. Later in the clinic we shall see, however, that it is possible to make observations which express this tendency, somewhat indirectly, in a quantitative manner.

Before taking up this problem of a quantitative index of dyspnea it will be well to review briefly some facts regarding the physiology and pathology of the circulation and respiration which bear on it. Perhaps the most fundamental activities in the body are the chemical processes which go on in the cells and tissues. These chemical processes, which may be broadly summed up under the head of "body metabolism," are the essential regulators of the circulation and respiration. In order that the metabolism may be carried on in a normal manner

certain substances must be brought to the cells and other substances must be carried away. Oxygen, for instance, is brought by the blood to the tissues from the lungs and carbon dioxide is carried away from the tissues and excreted through the lungs. The proper carrying on of this exchange of gases is absolutely necessary for the life of the cells, and the rate of the gas exchange depends on the rate of metabolism in the tissues. When a person is at complete rest and fasting, chemical activities in the tissues are low and the amount of oxygen needed by them is nearly at a minimum. If, however, the metabolism of the tissues is increased, as may occur, for instance, as the result of physical exercise or nervous excitement or certain disease processes, then the demands for oxygen become much greater. The increase of metabolism must be accompanied by a complex series of changes which result in an increased rate of flow of the circulation and an increased activity on the part of the lungs whereby more air is brought in contact with the blood in the pulmonary vessels. These adjustments on the part of the respiration and circulation go hand in hand, so that the need of the tissues for oxygen is supplied in the most economic way. It is obvious that an inadequate supply of oxygen to the tissues might result either from an insufficient circulation or an insufficient respiration. The blood must be properly aerated by the ventilation of the lungs, and it must then be transferred at the necessary rate from the lungs to the tissues. Both factors are important, and the failure of either will cause interference with the gaseous exchange which will manifest itself subjectively to the patient as the sensation of dyspnea. Dyspnea, therefore, may be caused either by failure of the heart to provide an adequate flow of blood or by failure of the lungs to properly aerate the blood. In patients with heart disease one would naturally expect the production of dyspnea to be particularly associated with an inadequate circulation of the blood. It is unfortunate, therefore, that there are at present no generally applicable methods for the determination of the rate of blood flow, and we have extremely little direct knowledge concerning the changes of blood flow resulting from decreased

efficiency of the heart muscle. More information has been obtained with regard to the respiration in heart disease and, as will be seen, there are certain pathologic changes in the character of the external respiration which can easily be demonstrated and which throw light on the occurrence of dyspnea in heart disease. It is with these changes that we shall concern ourselves especially in the present clinic.

When a normal person is lying quietly at rest his bodily activities are nearly at a minimum, and the amount of oxygen required by his metabolism is so small that it is easily supplied to the arterial blood by slow and rather shallow breathing. The minute-volume of pulmonary ventilation is low. When there is any increase in muscular activity the subject will require more oxygen, and the absorption of this additional oxygen, as well as the elimination of the increased carbon dioxide formed, is accomplished by an augmentation of the minute-volume of air which is brought into contact with the blood of the capillaries of the lungs. This rise in minute-volume is brought about by increase of both rate and depth of breathing. Thus, for instance, a man at complete rest may breathe 400 c.c. and at a rate of 15 per minute. His minute-volume is 6 liters. If he then undertakes strenuous exercise his metabolism will become greatly increased and the ventilation of his lungs correspondingly greater. The rate of respiration may be raised to 35 per minute and the volume per respiration to 1500 c.c. The total minute-volume will then be about 52 liters. This ability to increase the volume of air breathed per minute is fundamentally important in meeting the requirements of increased metabolism. It is, as you see, met in part by increased rate of breathing and in part by increased volume per respiration. The latter, however, is the more important means because it is more economic to take deep and slow respirations than it is to take rapid and shallow respirations. This depends on the fact that a part of each inspiration remains in the upper air passages or "dead space," and does not take any part in gaseous exchange. The ability of any individual to breathe deeply depends very largely on what is known as the "vital capacity" of the lungs. The vital capacity of the lungs is

the volume of a complete expiration after the deepest possible inspiration. It is easily measured by any simple form of spirometer, such, for instance, as the type which is commonly used in the gymnasium. In a normal individual the average vital capacity of the lungs is approximately 4500 c.c. It is obvious that when a person is exercising he is not able to take respirations which are equal in volume to his whole vital capacity. He cannot breathe his total vital capacity at a rapid rate. As a matter of practical experience it has been found that when subjects are exercising hard they breathe at a rate of approximately 35 per minute and they use about one-third of their vital capacity at each respiration. The greater the vital capacity, the more it is possible to increase the depth of respiration, and, conversely, the lower the vital capacity, the more one is limited in his ability to increase the depth of respiration.

A few years ago we carried on some interesting experiments at the Peter Bent Brigham Hospital on the production of dyspnea in normal persons and in patients with heart disease. On account of the danger of having patients with heart disease carry on severe exercise we allowed all the subjects to sit quietly in bed and produced the dyspnea by having them breathe air containing increasing percentages of carbon dioxide. The carbon dioxide stimulated the respiratory center just as it does when it is formed during exercise, and the rate and depth of respiration increased as the percentage of carbon dioxide in the inspired air was raised. At the end of the experiments with the normal subjects, when they were completely dyspneic, the volume per respiration averaged about three times as great as it was at the beginning. In the patients with heart disease, however, the results obtained were quite different. At the end of the observation, when they were extremely short of breath, it was found that they had increased the rate of breathing, but that the depth of breathing had changed comparatively little. This was particularly true in the patients who had marked evidences of cardiac weakness, but it was also true, to a less extent, in those in whom the cardiac lesion was comparatively well compensated. The fact that patients with heart disease did not react to the inspiration of

carbon dioxid by increasing the depth of their respiration in the same way as occurs in normal subjects led to an investigation of the general subject of the vital capacity of the lungs in heart disease. Ever since Jonathan Hutchinson made his first observations on the vital capacity of the lungs in 1846 it has been known that there is a decrease in the vital capacity in patients with cardiac weakness, but the subject had never been investigated thoroughly, and we were interested to find that the vital capacity of the lungs in heart disease bears a close relation to the clinical condition of the patient. This is especially the case if the clinical condition is judged by the tendency to dyspnea and, as has already been stated, the tendency to dyspnea is in the great majority of cases the most satisfactory index of the functional efficiency of the heart. In general, one may say that the lower the vital capacity of the lungs, the greater the tendency to dyspnea. The explanation of this is simple because, as we have seen, if the vital capacity is low it becomes impossible to increase the depth of breathing in a normal manner. As a consequence of this, when the metabolism is raised by exercise and a greater gaseous exchange is required, it is difficult to obtain the proper aëration of the blood by the lungs. The rate of breathing can be increased, but if the depth of breathing cannot be simultaneously increased, there must obviously be a great limitation to the extent to which the total minute-volume can be increased. Thus, while a normal person may be able to increase the minute-volume of pulmonary ventilation tenfold, a patient with heart disease was only able to raise his minute-volume two or three times above its value when at rest. Practical experience has shown that the vital capacity of the lungs varies with the general condition of the patient. If the clinical condition becomes worse and the patient becomes dyspneic with less exertion, the vital capacity will be found to have fallen, and, on the other hand, if the patient's general condition improves, the vital capacity will rise. It has, therefore, been found that repeated observations of the vital capacity give one an interesting and comparatively accurate means of following the course of patients with heart disease. Changes in vital capacity often indicate

more accurately than changes in physical signs or changes observed by other laboratory methods the course which the disease is taking. As will be seen from the patients to be shown, the vital capacity may be a good index of therapeutic action. Thus, for instance, the patient enters the hospital completely decompensated and with a very low vital capacity. Under digitalis his subjective condition improves and his vital capacity rises. After digitalization he may be given a prolonged rest cure, and during this period one can follow the vital capacity and see whether it gives further indication of improvement. While the patient is still being kept at rest in bed one can estimate fairly closely how much physical exertion he can undertake without undue dyspnea. It has been found, for instance, that patients who have a vital capacity which is at least 90 per cent. of the normal standards have no more dyspnea than do normal individuals. Those patients whose vital capacity is between 70 and 90 per cent. of the normal are somewhat handicapped and become dyspneic on moderate exertion, but they are usually able to lead quiet, normal lives. Patients with a vital capacity between 50 and 70 per cent. of the normal must be extremely limited in their activities and become dyspneic very rapidly. Those with a vital capacity below 50 per cent. of the normal are usually bed-ridden or extremely handicapped patients. The expression of vital capacity in forms of percentage of normal is an extremely useful method which allows one to generalize in a way that would otherwise be impossible. Unfortunately, it is not easy to obtain normal standards that are reliable in every case because there are so many factors which may cause variations in the vital capacity of the lungs. Among the most important of these are height, weight, age, and sex. West, however, working at the Peter Bent Brigham Hospital, found that the vital capacity bears a closer relation to body surface than to any other function, and, following his suggestion, we are accustomed to determine the normal vital capacity on this basis. The surface area is computed very easily by the method of Dr. DuBois from the height and weight. According to West, a normal man has a vital capacity of 2.5 liters per cubic meter of body surface area, and

a normal woman has a vital capacity of 2 liters per cubic meter of body surface area. These values apply to young adults and are probably fairly well applicable up to the age of fifty. Beyond this we know there is a decrease in the vital capacity of the lungs, but adequate figures for the later decades are still lacking. The deviation of normal individuals from these standards is usually not more than 10 or 15 per cent., although athletes may have a somewhat higher vital capacity. The cause of the decrease in the vital capacity of the lungs in heart disease presents a problem of some interest. In advanced cases, in which there is pleural effusion and pulmonary edema, it is easy to understand how the movements of the lungs would be interfered with and the vital capacity reduced. In a great many cases, on the other hand, there is apparently no relation between the decrease in the vital capacity and such physical signs. There may, indeed, be a considerable fall of the vital capacity in patients in whom the examinations of the lungs reveals absolutely nothing. A man with mitral stenosis, for instance, may give a history of dyspnea on walking rapidly or on going up stairs. Examination of his lungs by the usual methods and by the x-ray gives no indication of any pathologic lesion, but his vital capacity is found to be 70 per cent. of the normal. In such cases it has been suggested that the limitation of the movements of the lungs, which is evident from the decrease in the vital capacity, is due to an increased pressure in the pulmonary circulation with engorgement of the blood-vessels and a consequent interference with the elasticity of the lungs. It seems probable that some such circulatory abnormality is at least one cause of the low vital capacity in heart disease, and if the theory just stated is true, then the determination of the vital capacity of the lungs may give us important information concerning the condition of the pulmonary circuit. The low vital capacity is certainly not merely the result of general weakness, for we have found, from observations on patients with other diseases, such as pernicious anemia, in which there is much more profound general weakness, without involvement of heart or lungs, that the effect on the vital capacity is much less than it is in heart disease.

The following patients will illustrate concretely the manner in which the vital capacity of the lungs is of particular interest in heart disease: The first patient (Medical No. 15,373) is a woman thirty-five years old, who entered the hospital August 10, 1920, with the following diagnoses: Chronic myocarditis, auricular fibrillation, mitral stenosis, mitral regurgitation, pleural effusion. She had smallpox, diphtheria, measles, and mumps in childhood, and influenza and tonsillitis more recently, but there is no history of chorea, rheumatic fever, or scarlet fever. The patient is a Russian and speaks English with difficulty, but as far as could be made out she considered herself well until fourteen months previous to admission, at which time she had a miscarriage. After this she had to remain in bed for several weeks on account of palpitation, shortness of breath, dyspnea, and cough. She improved gradually, but ever since has done little housework and has usually been in bed in the afternoon. She came to the hospital on account of dyspnea, edema of the feet, and cough. On physical examination she presented the picture of a patient with a severely decompensated heart. She had dyspnea, slight orthopnea, and marked cyanosis. The heart was greatly enlarged and was absolutely irregular, at a rate of 114 per minute. Murmurs of mitral stenosis and mitral insufficiency were heard at the apex. There were râles at the bases of both lungs and signs of slight pleural effusion on the right side. The liver was greatly enlarged and extended down to the level of the navel. It was definitely tender on pressure. The systolic blood-pressure was 110 and the diastolic 80. Electrocardiograms showed auricular fibrillation and "right ventricular preponderance." Under rest and digitalis therapy the patient made little improvement. On August 20th she was still very short of breath. At this time her vital capacity was found to be 1000 c.c. Shortly after this her general clinical condition began to improve, whether or not on account of prolonged rest is uncertain, and in conjunction with this improvement the vital capacity rose to 1500 c.c., and then to 1700 c.c. At this time, thirty-one days after admission, the patient felt so much better that she was anxious to go home, and left the hospital. After the patient reached home she was able

to carry on a limited life with a fair degree of comfort for several months. She could do a little of her housekeeping, but had to rest frequently and avoid all the heavier work. She rarely went up stairs, as this produced marked shortness of breath. In such a manner she got along reasonably well until early in January, 1921 she "caught cold," developed a cough, and began to have so much dyspnea that she took to her bed for the greater part of the time. She made little improvement, however, and on February 4, 1921 again entered the hospital with much the same picture as on her previous admission, except that this time there was a more rapid heart and a marked "pulse deficiency," the heart rate being 120, with only 77 beats per minute palpable at the wrist. She was extremely short of breath and her vital capacity was 1200 c.c. Treatment was immediately begun with digitalis and she received 1.2 grams of powered digitalis within twelve hours after admission. The drug was then stopped because she began to show loss of appetite. Eight hours after the last dose of digitalis the heart-rate and the radial pulse-rate were both 48. There was remarkably rapid improvement in her general condition, with striking disappearance of the shortness of breath and edema. On February 15th the vital capacity had risen to 1800 c.c., and with continued rest in bed there was a further rise to 2100 c.c., and on March 1st to 2300 c.c. At this time the patient was perfectly comfortable and even when walking about the ward appeared to have no signs of cardiac insufficiency.

We may now turn to consider the chart (Fig. 195) which shows graphically the variations in the vital capacity of the lungs in this patient. It has been found that these records of the vital capacity are of much interest because they give a definite picture of the course of the patient's disease. None of the other clinical records, such as those of the pulse, temperature, respiration, blood-pressure, or diuresis, give such a comprehensive picture of the change in the patient's clinical condition. In the present instance, for example, none of these show anything of importance except the rapid drop in pulse-rate with digitalis therapy in the last period of decompensation and the associated

The second case is a man fifty years of age (Medical No. 15,213) who entered the hospital November 22, 1918, with the diagnosis of chronic myocarditis, auricular fibrillation, and chronic bronchitis. Except for an attack of "rheumatism" six years previously, at which time his knee and ankle were so swollen and painful on motion that he was in bed for five weeks, his past history is not important. Three years before entering the hospital, however, he began to suffer from palpitation of the heart and shortness of breath, both increased by exertion. He went to bed for six weeks and his symptoms improved to such an extent that he was able to be up and about until the present illness. For the last year his shortness of breath had been gradually increasing, and for the past two weeks it was so severe that he was unable to carry on his occupation as a ship carpenter. During this period he could not lie down at night because of dyspnea. He had no pain in the chest and gave no history of edema of the feet, but stated that for three weeks he had had a cough. On physical examination he was found to be slightly dyspneic even while at rest in bed. Examination of the heart showed great enlargement, with the left border on percussion 14 cm. from the midsternal line in the sixth interspace. The action of the heart was absolutely irregular in force and rhythm, but the rate was not rapid. At the apex a blowing systolic murmur of moderate intensity was heard. The radial arteries were tortuous and slightly thickened and the radial pulse was irregular in force and rhythm. The systolic blood-pressure was 110 and the diastolic 45. Examination of the lungs revealed nothing except a few crackling râles at the extreme bases behind. The edge of the liver was felt about 6 cm. below the costal margin in the right nipple line. It was smooth and slightly tender. There was apparently a small amount of fluid in the abdomen, but there was no edema of the legs. Under rest and digitalis therapy his condition improved rapidly, and after about three weeks he was discharged from the hospital feeling greatly improved. Unfortunately, no observations were made of the vital capacity during this admission. We have no more accurate index of his

rest at home he began to do a little work at a somewhat lighter job than he had previously held. In August, 1920, two years later, he was working regularly in a position which did not involve heavy exertion, and said that his heart did not bother him at all. At this time his vital capacity was 3500 c.c. His height was 175 cm. and his weight was 73 kilograms. On this basis his body surface area was 1.88 square meters, and the normal vital capacity for a man of this size would be 4700 c.c. His actual vital capacity (3500 c.c.) is 74 per cent. of the normal, and the amount of physical activity which he was able to carry on without dyspnea was apparently just about what was to be expected from a knowledge of his vital capacity. On January 14th the patient again came to the hospital and said that for two months he had been doing rather heavy work, but that one week previously he had had to stop on account of dyspnea which had progressively increased until the slightest exertion caused him great discomfort. At this time he was again sent into the hospital. He was moderately dyspneic even while sitting up in bed. The heart was larger than at his previous admission and the area of dulness extended 18 cm. to the left of the midsternal line. The action was absolutely irregular in force and rhythm and the cardiac rate was 90. There was a blowing systolic murmur at the apex transmitted into the axilla. A few moist râles were heard at the bases of the lungs behind, but otherwise the examination of the lungs was negative. The edge of the liver was felt 6 cm. below the ribs. There was slight edema of the ankles. x-Ray examination showed an enormously enlarged heart and extensive peribronchial infiltration of the lungs, but otherwise it was negative. At this time his vital capacity was 2400 c.c., or 51 per cent. of normal. It is interesting that the decrease in vital capacity from 3500 to 2400 c.c., which occurred from the time he was at work to the time when he entered the hospital with cardiac decompensation, was not associated with the development of any definite physical signs in the lungs. x-Ray examination did not show any fluid and the physical examinations never showed more than a moderate number of moist râles at the bases. Under rest and digitalis therapy he improved, and

at the end of three weeks he was discharged from the hospital. His vital capacity had risen to 2950 c.c., or 63 per cent. of normal. He was seen about two weeks later in the Out-patient Department, and at that time his general condition was much less satisfactory than it had been during the previous summer. This is quite in harmony with the fact that his vital capacity was only 2550 c.c., or more than 500 c.c. less than it had been. Unless the condition of his heart improves, so that his vital capacity becomes more than 63 per cent. of normal, he will probably not be able to do any more regular work. Since he has already had two serious breaks in cardiac compensation such a course seems to be unlikely.

These 2 cases illustrate the manner in which determinations of the vital capacity of the lungs are of value in following cases of heart disease. They aid us in estimating the functional condition of the heart because they give a direct indication of the tendency to dyspnea and a fairly accurate quantitative index of the changes in the tendency to dyspnea which are associated with the changes in the reserve power of the heart. They are thus a guide to prognosis and treatment. The vital capacity of the lungs gives a more satisfactory conception of the tendency to dyspnea than the patient's description of his own symptoms and is less affected by his subjective attitude. Some patients mislead us by understating and some by exaggerating their tendency to dyspnea. An interesting example of the latter came up recently when we were examining a neurotic patient who was an applicant for insurance benefits. He gave a history of extreme dyspnea on exertion and was apparently quite short of breath during the examination. Physical examination revealed a slight valvular lesion, but one that seemed in our opinion so wholly incapable of producing symptoms that the case was quite confusing. It was found to be perfectly normal. When the patient was requested a colleague to follow him and exercise when he did not know that he was being followed. The result brought back was that the patient was perfectly normal and apparently had no dyspnea.

undoubtedly in large part a malingerer who exaggerated all his symptoms, and it was the observation of the vital capacity that gave us the first direct evidence of this fact.

A decrease in vital capacity does not, of course, mean that a patient has heart disease. It may be due to many other conditions that interfere with the respiratory movements of the lungs. In pulmonary tuberculosis, for instance, the decrease in vital capacity seems to follow the increase of lung involvement very closely, and in such conditions as carcinoma of the lungs the vital capacity is often a better indication of the extent of the process than are the physical signs or even the x-ray examinations. In heart disease the vital capacity is of practical value after the diagnosis has been established and as an indirect index of cardiac reserve. On account of the fact that normal persons of the same size may show considerable variations in the vital capacity, the actual change in any given case is of more importance than the change in percentage of vital capacity as compared with the normal standards. In general, physical training may increase the vital capacity about 25 per cent. above the normal, and extreme physical weakness may reduce the vital capacity about 25 per cent. below the normal standards. Similarly, age, especially after fifty years, causes a decrease in vital capacity, but exact figures with regard to the amount of these figures are still wanting. In addition to this the chief drawback is the inability to make some patients co-operate satisfactorily, whether on account of failure to understand what is wanted or unwillingness to exert themselves. The latter is especially seen in neurasthenic patients. If the patient will not try to give his maximum expiration the observation is, of course, worthless. These difficulties are usually easy to recognize, however, and in spite of them the determination of the vital capacity of the lungs appears to be of considerable practical value in the management of patients with heart disease.

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Since the flora varies greatly in different localities and different seasons, it is essential for the physician who treats hay-fever to know the distribution and the seasons of pollination of the plants indigenous in the territory where his patients live—what plants are most common, which are wind-pollinated, and at what time the pollen is shed. In securing this information the co-operation of a field botanist who is familiar with the plants of the region is of value. With knowledge of the pollen habits of plants, most pollens are at once eliminated as probable causes of hay-fever, and only those plants which produce pollen in abundance during the hay-fever season, or to which the patient is directly exposed, need be considered.

By a careful history of the seasonal occurrence of the patient's hay-fever further elimination of probable causes can be made, because usually the time during which the patient has hay-fever corresponds closely with the season of pollination of a plant or groups of plants that is known to be the common cause of hay-fever in that locality at that time of the year; this indication as to the cause of the symptoms can then be verified by the skin tests with the pollens in question. The age of onset, the number of years' duration of hay-fever symptoms, and the sex of the patient do not have any bearing on the frequency, the cause, or the treatment of the condition.

In New England there are three distinct seasons of hay-fever which correspond with the periods of pollination of the groups of plants that are the common causes of hay-fever in that locality. The earliest hay-fever season, extending from the middle of March to the middle or last of May, and in late seasons through the first week in June, is caused chiefly by the pollens of trees. Beginning with the pollination of the hazelnut and witch hazel about the middle of March, pollen is shed in late March and April by the willow, the poplars, the junipers, maples, birches, and elms, and in May by the sweet fern and bayberry, the ashes, oaks, sycamore, hickories, walnut, alder, and the various fruit trees, and by the pines in late May or early June. The writer has observed 12 patients who were sensitive to and had hay-fever from the pollens of trees. One patient had hay-fever

caused by the pollen of apple blossoms and was free from symptoms following preseasonal treatment with apple pollen extract. One patient who was sensitive to the pollen of the oak and maple, and another who was sensitive to willow pollen, were both free from symptoms following treatment with these pollen extracts. Other patients were sensitive to tree pollens: 1 to poplar pollen, 1 to willow, 2 to ash, 2 to both willow and poplar, and 1 to willow, poplar, and ash. One patient who every year has hay-fever for a single day late in May at a time when he drives through pine woods was sensitive to pine pollen. Since cases of this very early hay-fever are comparatively rare, and the symptoms last usually from three to four days to two weeks at most, according to the period of pollination of the tree to which the patient is sensitive, it does not seem essential except in isolated cases to give treatment with tree pollens. The tree pollens to which patients usually give positive reactions and with which it is most frequently desirable to treat, are the willow, poplar, and maple.

The second season of hay-fever, usually called early or spring hay-fever or rose-cold, extends in New England from the middle or last of May to the middle of July, and the principal cause is the pollens of the grasses. Other plants, such as dandelion, buttercup, daisy, and sheep sorrel, pollinate at this time, but, with the exception of daisy, no patient when tested has been found sensitive to these pollens, and if they ever cause hay-fever it is by direct smelling of the flower. Still other plants, such as plantain, pigweed, smart weed, pepper grass, clover, and dock blossom during this season, but the amount of pollen produced is so small that it would be difficult to collect, and it is too small in amount to cause symptoms. Of patients tested with daisy pollen, 8.5 per cent. did not react with the whole pollen, 57 per cent. failed to react to the 1 : 100 dilution, 21 per cent. did react to the whole pollen, but not to a 1 : 500 dilution, 10 per cent. reacted to a 1 : 500 dilution, but not to any higher dilution, and only 3.5 per cent. reacted to a 1 : 1000 dilution; therefore in only 3.5 per cent. of the cases could the daisy be a possible cause. Moreover, these cases tested with the daisy had their symptoms during August and September, when ragweed pollinates, and no

symptoms during the time of daisy pollination; hence the positive reaction to the daisy is probably an expression of the botanic relationship between daisy and ragweed, which belong to the same family, rather than an indication of the cause of the symptoms. Rose, which pollinates at the time of early hay-fever, rarely causes hay-fever, because it produces little pollen and is pollinated by insects. Many persons who have early hay-fever suspect that rose is the cause because it is the conspicuous flower at this time, and for this reason skin tests must frequently be done with rose as well as grass pollen in order to satisfy the patient. Of 35 patients tested with rose pollen at their own request, 31 failed to react more strongly than what is called a doubtful reaction to the pollen of either red or white rose, and 2 who did give a positive skin reaction to the whole pollen did not react at all to a 1 : 100 dilution of rose pollen. One patient who was about equally sensitive to the pollens of three grasses and to rose pollen was practically free from symptoms following treatment with equal parts of red top grass and rose pollen extract. A second patient who was sensitive to rose pollen only was free from symptoms following treatment with rose pollen extract; this freedom from symptoms was repeated the following year, when a second course of treatment with rose pollen extract was given, even though she was a nurse in a hospital where she had to be intimately associated with roses. A florist who had hay-fever at any time of year, whenever he worked in a rose-house, was sensitive to rose pollen only, and was free from symptoms following treatment with rose pollen extract. In the four years during which grass cases were tested and treated, only 2 true rose-cold cases were encountered, and for this reason it would seem that in New England roses are rarely the chief cause of early hay-fever.

The grass pollen, which is the principal cause of hay-fever in New England during June and July, is produced in abundance, is light, and is carried far by the wind. One of the earliest grasses to pollinate in May is lawn grass, the short slender grass of cultivated lawns, but since hay-fever rarely starts early in May, lawn grass, in all probability, rarely causes hay-fever.

Lawn grass continues to pollinate at intervals throughout the summer, and in patients who are sensitive to many grasses and who are not sufficiently treated with one grass pollen to protect against others, lawn grass pollen probably aggravates the hay-fever symptoms. Orchard grass and many other grasses pollinate in June and July, each at its own particular season, but most of these grasses are not commonly encountered. The same 35 patients who were tested with rose pollen were also tested with orchard grass; 30 failed to give positive skin tests with the whole pollen, and the 5 patients who reacted positively to the whole pollen gave no reaction to the 1:100 dilution of the pollen extract, and hence were not sensitive enough to it to have hay-fever from exposure to orchard grass pollen. These tests indicate that orchard grass (*Dactylis glomerata*) is rarely the cause of hay-fever.

Corn, a member of the grass family, pollinates in July, and is a possible cause of early hay-fever, especially in those who cultivate and gather it, and to a less degree in those who eat it, since a small amount of pollen clings to the husks. Of 40 cases treated for early hay-fever who were tested with corn pollen, 22 failed to give a positive skin test with the whole pollen, and of the 18 who reacted positively to the whole pollen, all failed to react to the 1:100 dilution. The individual granule of corn pollen is very large and heavy, and it falls rapidly from the tassel at the top of the corn-stalk to the tips of the ears which it is to fertilize, and it cannot be carried more than a few feet by the wind. Hence intimate exposure is necessary for corn pollen to produce hay-fever, and treatment with corn pollen is usually not essential, because the patient, unless he is a grower of corn, can easily avoid it. For this reason corn can practically be eliminated as a cause of hay-fever except in localities where large fields of it are grown, and this is likewise true of the other grains, namely, wheat, oats, barley, and rye, which may be factors of importance in the grain-growing regions of the West.

By a careful analysis of the history of the patients, the early hay-fever season is subdivided into two shorter but distinct

periods; the first is the three weeks during late May and the first two weeks in June, and the conspicuous grass in pollination at this time is June grass (*Poa pratensis*), which sometimes begins to pollinate as early as the middle of May and stops by the middle of June, a few days to a week before the second and longer period of early hay-fever starts. A second period begins about the middle of June and continues for six weeks until the middle or end of July, and the chief grasses in pollination during this time (June and July) are red top (*Agrostis alba*) and timothy (*Phleum pratense*). Patients with early hay-fever must be tested, therefore, with the pollens of these three grasses. Those who have hay-fever only during June may be expected to react more strongly to June grass and less strongly or not at all to red top and timothy. Patients who have hay-fever in late June and July tend to react to both timothy and red top, usually more strongly to timothy, and less strongly to June grass. Patients who have hay-fever from late May to the middle or end of July usually react positively to all three grasses. Therefore, as has already been stated, patients with early hay-fever should be tested with the pollens of the three grasses, timothy, red top and June grass, and with rose pollen, since an occasional patient is more sensitive to one of them rather than to timothy, but about 90 per cent. of the early hay-fever cases can be treated satisfactorily with timothy pollen extract alone.

In regions outside of New England the exact times of grass pollination, and even the species of grass with which it is essential to treat may be different, although one patient who was treated with red top pollen extract had no trouble with hay-fever in Wyoming, and very little while he was in California. In some localities alfalfa may be one cause of hay-fever, since it produces pollen in abundance.

The majority of hay-fever patients in New England begin their symptoms between the 10th and 20th of August, the opening of the longest and most severe period of hay-fever, which extends from the middle of August to the first frost. The chief cause of the late or fall hay-fever is the pollen of the common ragweed (*Ambrosia artemisiæfolia*), sometimes called the

dwarf ragweed or Roman wormwood. The pollen is produced in enormous quantities and is so light and abundant that it rises in a yellow cloud when a pollinating plant is disturbed. The air at this season of the year, even in towns and cities, is laden with ragweed pollen, and the small, burr-shaped granules cling to other flowers, particularly golden rod and asters, to such an extent that these flowers which produce very little pollen of their own shed enough ragweed pollen when used for decorations indoors to cause symptoms in sensitive individuals. Many other compositæ, such as golden rod, golden glow, sunflower, aster, and cosmos, pollinate during August and September, but, like other compositæ, particularly the dandelion in the spring and the daisy in early summer, these flowers produce very little pollen and are pollinated by insects, and consequently they can cause hay-fever only by direct contact. Of a total of 120 patients who were tested with the pollen of golden rod, 12.5 per cent. failed to react to whole pollen, 66 per cent. failed to react to a 1 : 100 dilution of the pollen, 10 per cent. did not react to a 1 : 500 dilution, 8.25 per cent. did react to a 1 : 500, but to no greater dilution, and only 3.25 per cent. reacted to a 1 : 1000 dilution, but to none higher. Therefore, in only 3.25 per cent. of the cases could golden rod be assumed to be a possible cause of fall hay-fever. As in the case of the daisy, already discussed in this paper, the positive reactions to the pollens of compositæ other than ragweed, in patients that give a positive reaction to dilutions of ragweed pollen, are to be interpreted as an expression of botanic affinity between related plants rather than as an index of the cause of hay-fever. Only in cases where the reaction to ragweed is negative or nearly so is treatment with the pollens of other plants for fall hay-fever indicated. Four patients who gave more or less positive reactions to a 1 : 1000 dilution of daisy pollen were treated with extract of ragweed pollen, and as a result of the treatment 2 were free from symptoms and 2 were 75 per cent. benefited. Another patient who reacted to a 1 : 1000 dilution of corn pollen was 75 per cent. relieved by treatment with ragweed pollen extract. Of 3 patients who reacted more or less strongly to a 1 : 1000 dilution of golden rod pollen, 2 were

free from symptoms and 1 was benefited 75 per cent. by treatment with ragweed pollen; 100 patients were tested with sunflower pollen, and of these, 50 per cent. reacted positively to the whole pollen, but gave no reaction with the 1 : 100 dilution of the pollen, and 50 per cent. failed to react to the whole pollen. Therefore, pollens other than ragweed seem to play no important part in the cause of fall hay-fever in New England.

In different seasons there is great variation with regard to the abundance of pollen, and the time of beginning and ending of pollination; the prevalence of colds during or at the end of the hay-fever season may be interpreted as attacks of hay-fever and so mask really satisfactory results of treatment. In 1918 ragweed began to pollinate about August 8th, and heavy frost stopped the pollination about the middle of September; consequently, the hay-fever season began early and was very short. In 1919 the weather was so cold and rainy through September that pollination was below normal in amount, pollen was kept so wet that it could not blow about, and colds were frequent; the amount of pollen present in the air was so small as compared with normal seasons that hay-fever symptoms were comparatively mild, and sometimes colds were mistaken for attacks of hay-fever. In 1920 a hot, dry August was favorable for the development of ragweed, and since no hard frost occurred until late in October, pollination continued in profusion from about August 13th to October 1st, when the plant naturally finished the production of pollen and went to seed; consequently, the 1920 season was long and severe, with few colds, and in such a season the results of treatment are thoroughly tested. In the interpretation of results, particularly in comparing successive years, the seasonal variations and the condition of the patients, particularly with regard to the prevalence and susceptibility to colds, must be taken into consideration. In localities outside of New England the ragweed is apt to be a common cause of fall hay-fever, but the season of pollination varies in different places, and other plants that cause hay-fever may be common. Another species of ragweed called the giant variety (*Ambrosia trifida*) is rare in the East Central States and in New England,

but in the Middle West it is abundant and is a cause of hay-fever that must be reckoned with in regions where it grows. In the far West sage brush and tumble weed may need to be considered also. Distant localities must be investigated by those who are familiar with the flora of the region.

Although the principal causes of hay-fever in New England are the pollens of ragweed, timothy, and June grass, an occasional cause is the pollen of the rose, of red top grass, and of various trees. Since there is an almost unlimited supply of plants that may rarely cause hay-fever, for testing the occasional patient who fails to obtain satisfactory results from treatment with the common pollens, an extensive assortment of the rare pollens is desirable. Patients who are sensitive to ragweed should be warned not to smell of golden rod, golden glow, sunflower, aster, chrysanthemum, and other plants that pollinate during the ragweed season. Patients who are sensitive to the grasses should avoid close contact with clover, daisy, lily, dandelion, rose, lawn grass, orchard grass, and corn, if there is evidence that they are sensitive to these flowers. One less obvious but frequent result of treatment with the pollen to which the patient is most sensitive is the freedom with which the patient can go into the garden, walk in the fields, or smell of flowers that before treatment would have produced great aggravation of the hay-fever symptoms. In other sections of the country it may be necessary to treat with the pollens of cereal grains, with sunflower, or other common plants.

The leaves of some plants and trees or the fine hairs that make the pubescence on the under side of some leaves may cause hay-fever. One patient was studied who had hay-fever from, and was treated with, the hairs of the leaf of the willow, to which she gave a positive skin test, and symptoms were relieved after treatment with an extract of the leaves. Another patient of whom the writer has known was sensitive to and had hay-fever from the plantain leaf. Although seasonal hay-fever due to foods has not been noted by the writer, many hay-fever patients find that their symptoms are aggravated by certain foods that they can eat at other times without symptoms

when they do not have hay-fever, and that these same foods do not cause hay-fever during the usual hay-fever season if the patient has had sufficient preventive pollen treatment. These foods are usually the fruits, commonly the peach, melon and apple, and they bear no relationship to the causative pollen. Frequently eating green corn and the use of wine and beer aggravate ragweed hay-fever, but not hay-fever from grasses; sometimes celery acts in the same way. Usually it is the skin and not the flesh of the peach that produces symptoms, and cooking fruits renders them innocuous. Occasionally a patient with seasonal hay-fever fails to react to any of the common or rare pollens, and in such non-sensitive cases even an ophthalmic test and snuffing whole pollen or spraying concentrated solutions of pollen up the nose fail to give symptoms. In such cases the primary cause seems to be bacterial infection, and treatment with autogenous vaccines made from the nasal secretions is often effective in relieving the symptoms. During hay-fever seasons some individuals who are sensitive and have hay-fever from pollens also have vasomotor symptoms ranging from sneezing to asthmatic attacks, caused by odors from flowers that have no pollen or to the pollen of which the patient is not sensitive, particularly lilies, lilacs, hyacinth, sweet pea, honeysuckle, and peony. Such olfactory stimulants may be classified as mechanical, chemical, thermal, and odorific. Of the mechanical irritants, dust is the most common, particularly sweeping dust, hay dust, and street dust, and fine powders, such as talcum. Soap powder, lye, and ammoniacal fumes are frequent chemical irritants. Of the odorific irritants, heavily scented perfumes, face powders, musty air, and stable dust are the most frequent. Thermal irritants are sudden changes of temperature, as going from warm air to extreme cold, from moist to very dry air, and exposure to drafts; a frequent example is sneezing with or without running of the nose on arising and retiring. Usually these symptoms are relieved by treatment with the pollen to which the patient is sensitive.

The causes of hay-fever in New England have been discussed at length, with indications as to the pollen extracts that should

preferably at weekly intervals and never oftener than once in five days.

While the schedule of treatment calls for fourteen injections, modifications frequently have to be used. Sometimes a patient is so sensitive as to give a slight reaction to a 1 : 10,000 dilution of the pollen, and in that case an initial dose of 0.15 c.c. of the 1 : 20,000 is given, followed by one dose, 0.15 c.c., and sometimes a second dose, 0.25 c.c. of 1 : 10,000. Often it happens that a patient has considerable local or general reaction following some one inoculation in the schedule, making necessary the repetition of that particular dose before the next higher can be given. Often the patient comes for treatment too late to complete the scheduled series of inoculations before the onset of pollination, and for preseasonal treatment alone some of the final treatments in the schedule must be omitted. In some cases the second treatment with the 1 : 1000 dilution, namely, 0.25 c.c., is omitted, and in some cases instead of giving 0.15 c.c. of the 1 : 100 dilution, when this happens to be the final treatment that the patient can receive before the beginning of pollination, a fifth dose of the 1 : 500 dilution, namely, 0.55 c.c., is often substituted, and even a sixth treatment with the 1 : 500 dilution, namely, 0.65 c.c., is sometimes given. These larger doses of the 1 : 500 dilution approximate the amount of protein present in 0.15 and 0.2 c.c. of the 1 : 100 dilution; therefore, the fifth and sixth treatment with the 1 : 500 dilution is practically the equivalent of giving 0.15 and 0.2 c.c. of the 1 : 100 dilution. By far the greater number of patients are treated from three to five times with the 1 : 500 dilution, and since this number of treatments has given fairly satisfactory results, this number of treatments, a total of ten, seems to be worth giving, although a continuance of the schedule beyond three doses of the 1 : 500 dilution is desirable, and giving less than three treatments with the 1 : 500 dilution usually confers very little protection on the patient.

In order to complete the above schedule of fourteen treatments previous to the onset of pollination of the grasses and of the symptoms of early hay-fever during late June, treatment with the grass pollens should begin about March 1st, and if

tion as a diluent. These solutions are used for both skin tests and treatments, and with the addition of a small crystal of thymol they keep for months in a cool place. Solutions of pollen suitable for tests and treatment may be made by extracting the protein from the pollen, precipitating and drying, and using this pollen protein in the form of a dry powder to make the pollen solutions by weight, or the pollen solutions may be purchased from various drug houses, all prepared for tests and treatment.

The principal is to test the patient with the identical solutions which are to be used in treatment. The strong solutions will give a large reaction, and the size of the reaction diminishes in proportion to the decreasing amounts of protein present in the higher dilutions, until the reaction becomes doubtful, and finally a solution is reached which gives no reaction on the skin. This dilution to which the patient fails to react is the dilution with which it is safe and proper to start treatment.

From the experience of four seasons, a method of treatment consisting of fourteen injections of pollen solutions, given once a week in gradually increasing amounts, and terminating just before the time of onset of symptoms, has been found to give satisfactory results in a majority of cases. This preseasonal method of treatment with pollen extracts is as follows: The first dose consists of 0.1 to 0.2 c.c. of the strongest dilution that failed to give any skin reaction whatever, no matter how slight. The majority of patients gave a more or less positive reaction with the 1 : 5000 dilution, but frequently were negative to the 1 : 10,000 dilution; therefore the first treatment consisted of 0.1 or 0.2 c.c. of the 1 : 10,000 dilution. Treatment was given subcutaneously once a week in gradually increasing amounts, so that stronger and stronger dilutions were used as the treatment progressed, until one or more doses of the 1 : 100 dilution were given. The best outline for treatment for a patient who gives a more or less positive reaction with a dilution of 1 : 5000 of pollen extract is as follows: 1 : 10,000, give 0.15 c.c.; 1 : 5000, give 0.15 c.c., 0.25 c.c., 0.35 c.c., 0.45 c.c.; 1 : 1000, give 0.15 c.c., 0.25 c.c.; 1 : 500, give 0.15 c.c., 0.25 c.c., 0.35 c.c., 0.45 c.c.; 1 : 100, give 0.15 c.c., 0.2 c.c., 0.25 c.c., each dose to be injected

preferably at weekly intervals and never oftener than once in five days.

While the schedule of treatment calls for fourteen injections, modifications frequently have to be used. Sometimes a patient is so sensitive as to give a slight reaction to a 1 : 10,000 dilution of the pollen, and in that case an initial dose of 0.15 c.c. of the 1 : 20,000 is given, followed by one dose, 0.15 c.c., and sometimes a second dose, 0.25 c.c. of 1 : 10,000. Often it happens that a patient has considerable local or general reaction following some one inoculation in the schedule, making necessary the repetition of that particular dose before the next higher can be given. Often the patient comes for treatment too late to complete the scheduled series of inoculations before the onset of pollination, and for preseasonal treatment alone some of the final treatments in the schedule must be omitted. In some cases the second treatment with the 1 : 1000 dilution, namely, 0.25 c.c., is omitted, and in some cases instead of giving 0.15 c.c. of the 1 : 100 dilution, when this happens to be the final treatment that the patient can receive before the beginning of pollination, a fifth dose of the 1 : 500 dilution, namely, 0.55 c.c., is often substituted, and even a sixth treatment with the 1 : 500 dilution, namely, 0.65 c.c., is sometimes given. These larger doses of the 1 : 500 dilution approximate the amount of protein present in 0.15 and 0.2 c.c. of the 1 : 100 dilution; therefore, the fifth and sixth treatment with the 1 : 500 dilution is practically the equivalent of giving 0.15 and 0.2 c.c. of the 1 : 100 dilution. By far the greater number of patients are treated from three to five times with the 1 : 500 dilution, and since this number of treatments has given fairly satisfactory results, this number of treatments, a total of ten, seems to be worth giving, although a continuance of the schedule beyond three doses of the 1 : 500 dilution is desirable, and giving less than three treatments with the 1 : 500 dilution usually confers very little protection on the patient.

In order to complete the above schedule of fourteen treatments previous to the onset of pollination of the grasses and of the symptoms of early hay-fever during late June, treatment with the grass pollens should begin about March 1st, and if

treatment begins as late as April 1st, not more than the first three or four injections of the 1 : 500 dilution can be given. The importance of beginning preseasonal treatment with June grass not later than March 1st and with timothy and red top by the middle of March at the latest is indicated by the results of varying amounts of treatment, for in general it has been found that the greater the amount of treatment, the more complete is the relief from hay-fever symptoms. Of the 78 patients treated pre-seasonally with grass pollens, 36, or 46 per cent., were free from symptoms, 11, or 14 per cent., were practically free, 17, or 21 × per cent., were 75 per cent. relieved, 11, or 14 per cent., were 50 per cent. benefited, and 3, or 4 per cent., were not improved. The writer concludes from his experience that, although timothy pollen is the chief cause of early hay-fever and sufficient treatment with timothy pollen extract alone gives excellent results, all patients should be tested with the pollens of June grass, red top, and rose, as well as timothy, because an occasional patient who is more sensitive to one of these other pollens than to timothy, may need treatment with them rather than with timothy pollen. A patient who is equally sensitive to timothy and red top should be treated with timothy pollen extract alone because the two grasses pollinate at the same time, timothy is the more prevalent, and timothy pollen will protect against red top exposure, provided two or more treatments are given with the 1 : 100 dilution. Sufficient treatment with timothy pollen extract alone would also protect against June grass exposure, but since June grass usually pollinates comparatively early in the course of treatment with timothy pollen, before the larger and more effective doses have been given, the patient who is sensitive to June grass has more or less severe symptoms in late May and early June during the time of June grass pollination. Unless treatment with June grass pollen is started earlier than it is customary to start treatment with timothy pollen, not enough June grass pollen can be given before the time of June grass pollination to protect against June grass exposure. Treatment with a mixture of June grass and timothy pollen extracts retards and diminishes the amount of treatment that might be

given with either one alone, because the patient more frequently has a sore arm, and has symptoms of hay-fever in late May and early June that are really caused by exposure to June grass, but may be considered as due to the treatment, with the result that doses of timothy pollen are repeated when it would be safe to give the next increase in amount, thus cutting off some of the more important doses at the end of the schedule and causing incomplete protection against red top and timothy. Therefore, preseasonal treatment with pollen mixtures seems advisable only in rare cases. It is possible to treat patients who have symptoms in June and July, and who are equally sensitive to June grass and timothy, by a combination of preseasonal or preventive treatment with timothy pollen extract alone, and curative or during the season treatment with minute amounts of June grass pollen extract given four or five times when the pollination of and symptoms from June grass first begin.

Frequently a patient presents himself for treatment after the symptoms have set in. Treatment of the patient with the pollen that causes his hay-fever during the time he is exposed to the pollen present in the air he breathes, particularly treatment with large amounts of pollen, would seem on the basis of anaphylaxis to result in danger of an overdose of pollen due to the combination of the injected and the inhaled pollen, thereby increasing rather than relieving the hay-fever symptoms. Nevertheless, although during the season or curative treatment is hazardous because there is no way of controlling the amount of pollen that is inhaled, this method of treatment is worth trying provided it is given with sufficient care and the skin test is used as a guide to the initial dose, as in the initial dose of preseasonal treatment. For instance, if the patient gives a positive reaction with the 1 : 10,000 dilution, but fails to react to the 1 : 20,000 dilution, he is given of the 1 : 20,000 dilution of pollen extract a dose 0.15 c.c., and five or seven days later 0.25 c.c.; then the 1 : 10,000 dilution, doses 0.15 and 0.25 c.c. Usually only four or five doses are given, and the same five- or seven-day interval is observed as in the preseasonal treatment. Although a few patients are entirely relieved by during the season treatment, and as many

more are 75 per cent. benefited, many are only slightly relieved, and nearly half of the number are hardly improved at all, so that it is a question whether this method of treatment is worth doing if the patient can go to a locality where his cause of hay-fever does not exist. The results of during the season treatment are markedly poor in comparison with the results of preventive treatment. If during the season treatment is given with June grass pollen extract during late May and early June, after the patient has developed symptoms from June grass exposure, the treatment with timothy pollen is continued according to the schedule of preseasonal treatment except that the June grass pollen extract and the timothy pollen extract may be mixed in the syringe and given as one injection, provided each dose is measured with care.

Preseasonal treatment of fall or late hay-fever follows the same schedule of dosage as that outlined for spring or early hay-fever, with the exception that treatment with ragweed should begin late in April or early in May in order to complete the schedule of treatment with ragweed pollen, just previous to the shedding of ragweed pollen between August 10th and 20th. Beginning ragweed treatment as late as the first week in June limits the treatment to from three to five injections of the 1 : 500 dilution. Of 439 patients treated preseasonally with ragweed, 25 per cent. were entirely free from symptoms, 20 per cent. were practically free, 32 per cent. were 75 per cent. benefited, 18 per cent. were 50 per cent. relieved, and $4\frac{1}{2}$ per cent. were not improved. In the case of 1 patient who was not benefited, the skin test with ragweed was as strong after as before treatment, and in whom the last injection produced an anaphylactic shock manifested by urticaria, and in 3 other patients who gave positive skin tests with a 1 : 1000 dilution at the end of treatment in spite of the fact that they had received one or more doses of the 1 : 100 dilution, the apparent desensitization of the skin did not progress with the increasing amounts of treatment. It is probable that, for some unknown reason, the mucous membrane also was not desensitized or that there was lack of union between the patients' antibodies and the pollen treatment acting as an an-

tigen. Two patients who were treated two and four times respectively with the 1 : 100 dilution failed to react at the end of treatment to all dilutions higher than the 1 : 100, and still were not benefited by the treatment. So that even with sufficient preseasonal treatment and apparent desensitization of the skin, as indicated by skin tests, there are a few hay-fever patients who are not benefited by preseasonal pollen therapy. In two-fifths of the cases the skin test at the end of treatment as compared to the skin test before treatment was decreased one hundred times, and in the remaining three-fifths of the cases, the skin test was diminished at least twenty times. In general, the larger the number of treatments given, the greater was the decrease in the sensitivity of the skin of the patient as indicated by the skin test, and the more nearly complete was the relief from symptoms. Further evidence of the more complete relief derived from larger amounts of treatment is shown in patients who are treated several years in succession. Usually a patient who is more or less benefited one year by insufficient treatment is completely relieved by sufficient treatment in another year. Favorable results follow any number of successive years' treatment, provided the average number of treatments is given each year. No matter how many successive years the patient is treated, approximately the same amount of treatment with the final dilution of the pollen extract is required as in preceding years, but no greater amount is necessary in succeeding years.

Still another method of treatment, which has been used with success by various investigators, is particularly adapted to patients who apply for treatment some time before the onset of their symptoms, but too late to complete the full schedule of preseasonal treatment. The initial doses of preseasonal treatment are given as usual, but instead of stopping all treatment when pollination and symptoms begin, the increasing doses are continued according to the schedule right through the hay-fever season. The results of this method of treatment, while not so good as those from sufficient preseasonal treatment, are more satisfactory than the results of during the season treatment alone, in that while few patients were entirely free from symp-

toms, one-third of the cases were 75 per cent. benefited, and nearly one-half of the cases were 50 per cent. improved, and only one-tenth of the cases received no benefit. It would seem fair to say that this method of treatment is preferable to during the season treatment alone, but not as effective as the regular pre-seasonal treatment which is begun early enough to permit its termination just before the onset of pollination.

Multiple sensitization to pollens, as has already been indicated, is a fairly common phenomenon, and frequently patients who have hay-fever nearly all summer, except for a slight pause during the first two weeks in August, are sensitive to the grass pollens and also to ragweed. The best treatment for these patients who have both early and late hay-fever is to start with timothy pollen extract alone, if timothy is the proper pollen with which to treat the early hay-fever, at the customary time in March, and follow the schedule of increasing doses until the customary time to begin treatment with ragweed pollen extract late in April. The ragweed treatment for fall hay-fever is then instituted and carried on independently of the timothy pollen extract treatment, except that the two pollens are given together in the same injection until just before the onset of timothy pollination. At that time the timothy pollen is stopped entirely and the ragweed continued alone up to the usual time for completing it, just previous to the pollination of ragweed. This method of treatment with mixed pollens is less satisfactory than treatment with either pollen alone, because to some extent each diminishes and retards the effect of the other pollen, doses have to be repeated more frequently, and it is difficult or impossible to give during the season treatment with June grass pollen, even though the need of treatment with June grass pollen is indicated by the symptoms and sensitivity of the patient.

The time of stopping pre-seasonal treatment varies somewhat with the earliness or lateness of the seasons of pollination, the variations of which from year to year have already been described. When the pollen develops earlier than usual, it may be necessary to stop treatment before the last few doses have been given, for fear of symptoms from an overdose when the

pollen is inhaled. Correspondingly, when the season of pollination is delayed, it is sometimes desirable to give another dose or two after the usual time of terminating the treatment, because the pollen is not yet present in the air. In localities outside of New England the seasons of pollination differ and the time of beginning treatment must vary in consequence, and the causative pollen may vary also. If treatment is given for the tree pollens in early spring, it should start in January or February.

When patients have seasonal hay-fever primarily from bacterial infection, relief of the symptoms is secured in a number of cases by treatment during the season with autogenous vaccines made from the nasal secretion; this comparatively rare type of non-sensitive seasonal case has been described earlier in the paper. In patients who are sensitive to and treated preseasonally with the appropriate pollens, bacterial infection of the irritated mucous membrane may be a secondary cause of symptoms during the season, and perhaps even more frequently the symptoms are continued by bacterial infection long after the termination of the time of pollination. Treatment with autogenous vaccines made from the nasal secretion after the onset of symptoms, or sometimes even treatment with stock vaccines of streptococci or *Staphylococcus pyogenes aureus* or *albus*, may give relief.

Some patients find it more convenient to spend the hay-fever season in some region where the plant that causes their symptoms cannot grow, than to take the course of preventive treatment. To escape ragweed hay-fever one must go to a place of such high altitude or so far north that the climate is too cool for the growth of ragweed, as at Bethlehem, N. H., Nova Scotia, and parts of Canada. It is difficult to avoid grass pollen except by a long sea voyage, or possibly in some arid regions of the southwest, but one may to some extent escape the particular species of grass to which one is most sensitive by going to a distant part of the country where for a season or two the patient may not develop symptoms from exposure to the pollens of the grasses indigenous to the new locality.

CONTRIBUTION BY DR. C. W. McCLURE

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TREATMENT OF FUNCTIONAL GASTRO-INTESTINAL DISTURBANCES¹

PATIENTS complaining of symptoms referable to the gastro-intestinal tract may be classified into five groups: (1) those with primary organic disease of the alimentary canal, such as benign ulceration, cancer, tuberculosis, etc.; (2) those in which gastro-intestinal symptoms are secondary to some definite organic disease outside the alimentary canal, such as nephritis, cardiac disease, pulmonary disease, constitutional diseases, etc.; (3) those rendered toxic by the introduction into the system of poisons, such as lead, mercury, etc.; (4) those with the so-called functional conditions; and (5) certain rare, serious conditions for which no definite cause can be found and the symptoms of which simulate those of organic disease.

Functional gastro-intestinal conditions are those for which no organic basis has so far been determined. Many of them are very common, but in spite of this their nature is but little understood. Their manifestations vary from mild to severe. Their prognosis as to life is almost invariably good, although a certain number end fatally, usually as the result of the failure of the patient to take sufficient nourishment.

Not infrequently in children acute gastro-intestinal disturbances occur, which are of short duration and do not lead to serious results. Usually they are, either correctly or incorrectly, ascribed to dietary errors. Such acute conditions in adults are not so frequent as in children, although they do occur. When

¹From the Medical Clinic of the Peter Bent Brigham Hospital, Boston, Mass.

met with in adults they often lead to the suspicion of some obscure, underlying organic basis.

In adults there is a well recognized group of chronic, functional, gastro-intestinal disturbances, in which the usual dietetic and drug treatment is very often unsatisfactory, as is evidenced by the chronicity of the symptoms in spite of the use of such measures. For purposes of description the group will be subdivided into the fatigue, suggestible, and habit groups; and a method of treatment will be discussed which has given very satisfactory results in these groups.

FATIGUE GROUP

The etiologic factor of this group is considered to be the depletion of physical reserve resulting from "wear and tear" on the organism. Patients belonging to this group have lost more or less of their physical reserve power and their sense of well-being, and often complain of malaise, lassitude, and other unpleasant sensations besides those referable to the gastro-intestinal tract. All of these manifestations are grouped under the term "fatigue." It is well recognized that temporary fatigue, resulting from either muscular or mental exertion, may be expressed as backache, aching of one or more sets of muscles, nausea, vomiting, headache, lack of power to concentrate the attention, blurring of vision, etc. All the manifestations of such acute fatigue disappear after rest. Long continued causes for fatigue, or short, violent causes, may give rise to long-continued manifestations of fatigue. It is on this basis that the symptoms present in this group are treated. The usual causes for fatigue are "the high tension type of life"; business, financial, or family worries; and grief due to deaths, disappointments, etc. In some of the patients it is difficult to elicit the cause for the presence of fatigue. The patient, as a rule, believes some organic disease exists and makes no mention of causes for fatigue. Not infrequently patients are very reticent about disclosing matters of a personal nature. By gaining the patient's confidence to a sufficient extent in such cases or by a close study of the patient's habits, business affairs, mode of life, etc., a very evident cause finally can be

obtained for what was previously a very puzzling condition; on the other hand, certain patients are not aware of the existence of factors which are producing fatigue. But after their attention is directed to the matter they are often able to show its presence.

The following case illustrates this group and is an example of the expenditure of an excessive amount of energy: The patient was a salesman, aged thirty-two. The family history and past medical history were unimportant. From February to November, 1914 the patient had had attacks of slight dizziness, with some nausea, and occasionally vomiting, but no hematemesis, bloody or tarry stools. The attacks recurred every two or three weeks and lasted about half a day. In November, 1914 severe epigastric burning from two to three hours after meals began; this symptom persisted for two weeks. The patient was then placed on a diet for peptic ulcer by a New York physician, which was followed for several months, finally with complete relief from symptoms. He remained well until the present illness (October, 1919). About the first of that month the onset of mild burning in the epigastrium, two to three hours after meals, began. The symptoms gradually increased in severity until at the end of three weeks the patient sought medical advice. The appetite was good. There had been no vomiting. The bowels were constipated. There had been no loss of weight.

Physical examination was essentially negative. By x-ray examination the stomach was normal in position and tone. Its outlines were regular. There was active peristalsis, and the pyloric sphincter closed normally. There was constantly present a definite irregularity of the lesser curvature side of the first portion of the duodenum. Otherwise the duodenum appeared normal. x-Ray studies were repeated two days and again one month later. On both occasions the duodenum filled normally and its outline was regular.

Gastric analysis was not done. The stools gave a negative benzidin test for blood. The usual examinations of the urine and blood were negative. The Wassermann reaction in the blood-serum was negative.

On the first visit the patient felt sure there was no cause for fatigue in his case. The patient studied himself during the next week. He discovered that, in going from office to office, he would almost run, and yet there was no cause to hurry; that his body muscles were held very tensely; and that he grasped the handle of his light valise so firmly that an impression of it was left in the palm of the hand. In other words, this patient was really expending a large amount of energy. By preventing this undue expenditure of energy the patient quickly became free from symptoms and has remained so.

SUGGESTIBLE GROUP

From this group the evident psychasthenic patient has been excluded.

Patients of this group are of an apprehensive and suggestible state of mind as regards the condition of their health. The onset usually follows an erroneous diagnosis, of more or less serious import, when the patient consults a physician for some trivial ailment; or the prescribing of medicaments leads the patient to believe he has some organic disease, or strengthens a suspicion of organic disease already entertained by the patient. Other common causes are ideas gleaned from reading books on medicine, or those dealing with the subject of physical health. These patients apparently do not conjure up symptoms, but sensations arising in the abdomen draw their attention to the gastro-intestinal tract. The explanation of the origin of these sensations may possibly be that patients either recognize sensations which occur normally, but are not normally cognated, or they exaggerate and react violently to sensations which in normally reacting persons are discarded. Whether or not either explanation is correct is undoubtedly questionable; but its understanding does allow patients to train themselves out of their symptoms so that the latter no longer disturb them.

The following case is cited as an example: The patient, a male clerk, aged twenty-two, entered the hospital complaining of "gas and pain in the stomach." The family history was essentially unimportant. The patient had had gonorrhea in

1916. The onset of the present illness had begun two years prior to admission to the hospital. During this period he had been under observation in the Out-door Department, during which time he had received various kinds of medication without relief. The onset of the symptoms began with cardiac palpitation and a sensation of precordial pressure. At that time his physician gave him some medicine which made his "stomach feel raw inside." Thereupon he began to have marked gaseous eructations, which finally would be associated with palpitation, epigastric distress, and occasionally vomiting. These symptoms were most severe about one hour after meals, and were relieved temporarily by food or soda. Two months before admission the onset of mild needle-like pains one hour after meals and in the region of the umbilicus occurred, and during the last two weeks of this period gas, belching, epigastric distress, and the pain were continuously present.

The physical examination was essentially negative. x-Ray studies of the gastro-intestinal tract showed nothing abnormal. The fasting gastric content was 12 c.c. in amount, and contained no food remnants, blood or acid. After an Ewald test breakfast free HCl was 24 and total acidity 50. The stools contained no occult blood. The Wassermann reaction in the blood-serum was negative. The usual examinations of the blood and urine were negative.

The patient was admitted to the gastro-intestinal clinic of the Out-door Department in July, 1919. Under treatment he improved rapidly over a period of two weeks. He then became engaged to marry. Having had gonorrhea, he consulted a physician as to a possible residue of that disease. The physician informed him that he had prostatic disease and it would take \$75.00 to cure him. The genito-urinary service of the hospital pronounced the patient free from prostatic or other disease. Nevertheless, the patient was so upset and worried by the local physician's diagnosis that he took the treatment. His gastric symptoms immediately returned in full force. After cessation of the treatment, temporary, partial recovery was again induced. At this period the patient slept in a store as a watchman during

the Boston Police strike. The position caused much excitement and apprehension on the part of the patient, and he again relapsed. During the next month the patient became free from symptoms and remained so several months later.

HABIT GROUP

There is a group of patients who seem to have trained themselves to reproduce symptoms. The explanation for this phenomenon may be given on the basis of normal psychology, as follows: Some emotional disturbance, such as death in the family, or a period of physical and mental strain, occurs. The patient's organism becomes fatigued and this gives rise to symptoms. On the other hand, possibly some organic or toxic condition, or a surgical operation gives rise to symptoms. In either event the constant presence of symptoms trains the attention of the patient to observe physiologic processes and he becomes consciously sensitive to these stimuli. He, therefore, acquires the habit of reacting more readily and much more violently to stimuli; and this gives a basis for the reproduction of symptoms after the initial cause for them has disappeared.

The following case illustrates the habit of reacting violently to external stimuli. The patient, a female aged thirty, had had grand mal epileptic seizures since the age of nineteen years. These were becoming less frequent, four attacks having occurred during the past year. Otherwise the past medical history was unimportant. The present illness began as the "vomiting of early pregnancy." Later the woman miscarried, but the vomiting persisted, occurring at least once a day. Vomiting was produced as the result of the sight or odor of food, as the result of riding on the train or street cars, or as the result of some trivial breach of etiquette at the table.

The physical examination was essentially negative. Examination of the urine was negative. Wassermann of the blood-serum was negative.

The patient's condition was explained to her as a habit neurosis. At the end of the first week of treatment she had not improved. She was then placed at rest in bed and given in-

creasing quantities of milk. During the first week of this treatment vomiting ceased. After three weeks the patient was allowed out of bed part of the day and given an increasingly liberal diet. For the next two months vomiting was still absent, although the patient remained rather easily nauseated. At the end of this time she very narrowly escaped being burned to death in a fire. This again caused the onset of vomiting, which persisted for about four weeks before the patient could master it. During the next two months nausea, but not vomiting, was easily produced, but was progressively growing less frequent in its occurrence, until after a period of several months it disappeared; and then the patient was symptom free.

The nervous system of the patient whose case has just been cited had become trained to produce vomiting during pregnancy, and this persisted after the latter had terminated. It finally became so keenly trained that the slightest breach of etiquette or emotional disturbance set up the proper reflex, and vomiting occurred. In other words, the vomiting was the result of violently exaggerated reaction to a mild stimulus, which had become a habit.

The reproduction of a certain single gastro-intestinal symptom seems to become a habit with some patients. By not permitting themselves to belch, a number of patients have broken up the habit of doing so. The following case makes it seem probable that the frequent passing of flatus may be the result of habit acquired by certain patients.

The patient, a male printer, aged fifty, complained of the frequent passing of foul-smelling flatus. The family and past medical histories were unimportant. He had been operated upon for left inguinal hernia in 1919.

The patient had been troubled with the passage of flatus and occasionally with pyrosis since the age of twenty years. During the past year prior to consultation the onset of fairly severe, abdominal colic began. The colic occurred only early in the morning, and persisted for from fifteen to twenty minutes. The patient was not constipated. His appetite was good. There had been no belching, regurgitation, vomiting, bloody or tarry

stools, or jaundice. He had lost 9 pounds in weight in six months' time.

The physical examination was essentially negative. The Wassermann reaction in the blood-serum was negative. The usual examinations of the stools, urine, and blood were negative. Two examinations of the urine (one by Dr. W. Denis, Massachusetts General Hospital) did not show the presence of lead.

After careful study the patient was told of the possibility of lead-poisoning causing his symptoms. It was then explained that the strain of his work (which the patient had said was present), long working hours, and no vacations might possibly be a factor in producing the abdominal pain. Passage of flatus was explained as a habit. He was instructed not to allow flatus to be passed, to take a three weeks' vacation, to eat a liberal, general diet and to keep his mind off his symptoms. During the vacation period 10 pounds were gained in weight and the colicky pain became much less frequent and less severe. Flatus was passed as usual. After a period of five weeks the colicky pain disappeared entirely and the patient had broken the habit of passing flatus. He remained free from symptoms two months later.

After a considerable period of observation this patient's condition was assumed to be entirely functional in origin, and under appropriate treatment he became free from symptoms.

Belching, as it ordinarily occurs, is not the result of antiperistalsis, as is readily shown by x-ray studies. Certainly the frequent passage of flatus is not always due to colonic peristalsis; for the latter occurs only at intervals of several hours. These facts lend support to the view that both belching and the frequent passing of flatus are probably due to the increase of intra-abdominal pressure brought about by voluntary factors, *i. e.*, contraction of the muscles of the abdominal wall. If this explanation is correct, it is readily understood how such symptoms can be abated. In this connection it may be well to state that both the stomach and the colon always contain considerable quantities of air.

TREATMENT

The plan of treatment which has been followed was developed as a natural sequence to the etiology of the groups which have just been discussed. The principles of therapy consist of eliminating unnecessary factors which produce fatigue and of retraining the nervous system to a rational psychologic state. Undue mental impressions and subtle methods for deceiving the patient not only have no place in therapy, but actually defeat the end in view. Because of the complexity of individual cases it is usually found best to combine the two principles of therapy in the treatment of a given case. The first step consists in eliminating possible causes. This elimination can be done only by the patient; that is, the patient must learn to work and to live his daily life without unnecessary expenditure of energy, and he must, also, train himself not to react in an exaggerated manner to stimuli. The latter means that the patient teaches himself to feel no longer the sensations which have given rise to his symptoms. The patient accomplishes this by attempting not to allow his attention to center on symptoms when they occur and not to be alarmed by them. In order that treatment be successful the patient must first thoroughly understand the nature of his condition, even to the minutest details. In actual practice my plan has been to see patients at weekly intervals. On these visits I explain to the patient, over and over again, my understanding of the case. When he once understands the cause of the symptoms and the factors at work in his own case, and acquires a fair understanding of physiopsychology and the causes for fatigue in general, then he is in a position to cure himself. In epitome the entire system of therapy is an educational process. The physician teaches, the patient learns, and then trains himself to apply what he has learned. The success of this method of therapy presupposes, at least, a fair degree of intelligence on the part of the patient. But the success obtained in some ignorant patients has been amazing.

Drugs and Diets.—The plan of therapy outlined above makes no mention of the use of drugs and dietary measures. Nearly all of the patients studied had received drug therapy prior to

their treatment by the plan here outlined. Certain of them had consulted many physicians, one of them as many as 100 physicians, and had had four hospital entries during the twenty years of his illness; all without relief. There is no doubt but that symptoms can be ameliorated and appetite increased by the proper drugs. But a cure was not effected in any of the patients of this series by their use. Furthermore, in these patients drug therapy often serves to convince the patient that he is organically diseased. Another reason for not using drugs is the fact that, when his symptoms are ameliorated, the patient is not forced to learn how to conserve energy and to train himself out of his symptoms. Because of this it was feared that drug therapy would defeat the end in view.

Certain patients, having tried various dietary measures without relief, will cease their use. One patient under my care, a well educated and intelligent man, had been unable to eat pork products for fifteen years without producing severe vomiting. Various patients restrict their diet by eliminating certain varieties of food, while many live on milk, toast, crackers, cereals and eggs. The reason for eliminating various kinds of food from the dietary is that the patients believe that these particular foods aggravated the symptoms. A study of the various food elements which had been eliminated from the diets of such patients showed no consistency in the kinds of foods avoided; in fact, most of the foods commonly eaten were eliminated from some one of the diet lists. This finding is comparable to the statements, concerning the types of diet to be used, in works on dietotherapy (Fitch). Different authors will use very different diets in the same type of case. A striking fact concerning these diets is that their use is based on the chemical factors of normal digestion or on ideas concerning gastric motility. The great majority of authors do not seem to have questioned the patient's observations as regards the production of symptoms by certain food elements. In other words, they have assumed that patients were capable of making accurate experimental observations and correct deductions from these observations.

Most patients can be treated in the hospital and should be immediately placed on the diet. It is essential that the diet being taken is indeed all that is necessary and that the patients positively stated agree to the program. Throughout the entire period of observation the patients are under the diet. At the end of the first week a number of patients are better or have been made somewhat better. Some have disappeared. In one patient the symptoms were somewhat aggravated for a period of a few days. The diet was persisted in, and at the end of the second week as a result of training or of betterment of general condition all symptoms disappeared. The patient mentioned above in whom pork products caused vomiting began eating them three times a week, during the third week of the treatment; no untoward symptoms were produced. It should be stated that often patients are alarmed when they are asked to eat a liberal, general diet. It is only by gentle persuasion that they can be induced to take the diet. In some of the patients I have had to promise either to call in person or send an ambulance for them should the diet cause serious trouble before they would agree to eat. One quite intelligent patient actually laughed at the idea that food would not seriously aggravate his symptoms. Nevertheless, the symptoms were not aggravated by the eating of a liberal, general diet. From such experiences it may be inferred that the use of special dietary measures in conditions such as represented by the patients of this type are unnecessary. They are harmful inasmuch as they may serve to make patients believe that they have organic disease.

The degree of gastrospasm in the 5 patients studied was well marked. 4 of them became free from symptoms without the use of abdominal support of any kind. The fifth case was an abdominal case without my knowledge. After the removal of the patient remained free from symptoms.

Anorexia occurred as another feature of interest. It was overcome in all patients.

patients were instructed to place before themselves at each meal a quantity of food which they considered large for a normal person; they then ate that quantity. That this was actually done cannot be proved, since the patients were not under observation at mealtime; but the statements of these patients are considered to be reliable. These patients finally developed good appetites. But whether this was the result of training or of betterment in their general condition is a question.

A word should be added concerning constipation. The great majority of the patients seen complained of constipation. But after excluding the use of cathartics, suppositories, enemata, etc., constipation was not found to exist. In comparatively few instances an enema every two or three days was necessary for a period of not more than a few weeks, after which the bowels regulated themselves. This discussion merely illustrates that in order to be sure that the patient, who states he is constipated, is a competent observer the physician must observe for himself.

Cathartic drugs and measures such as enemata are usually harmless in themselves, other than affording a means of centering a patient's attention on himself, and this is frequently undesirable. There are, however, occasionally developed unpleasant abdominal symptoms as the result of the prolonged use of cathartics. This is illustrated by the following case report:

During the past thirty years the patient, a male, aged fifty-eight, had taken some one of the cathartic drugs almost every day because he believed himself to be constipated. Otherwise the past medical history was essentially negative.

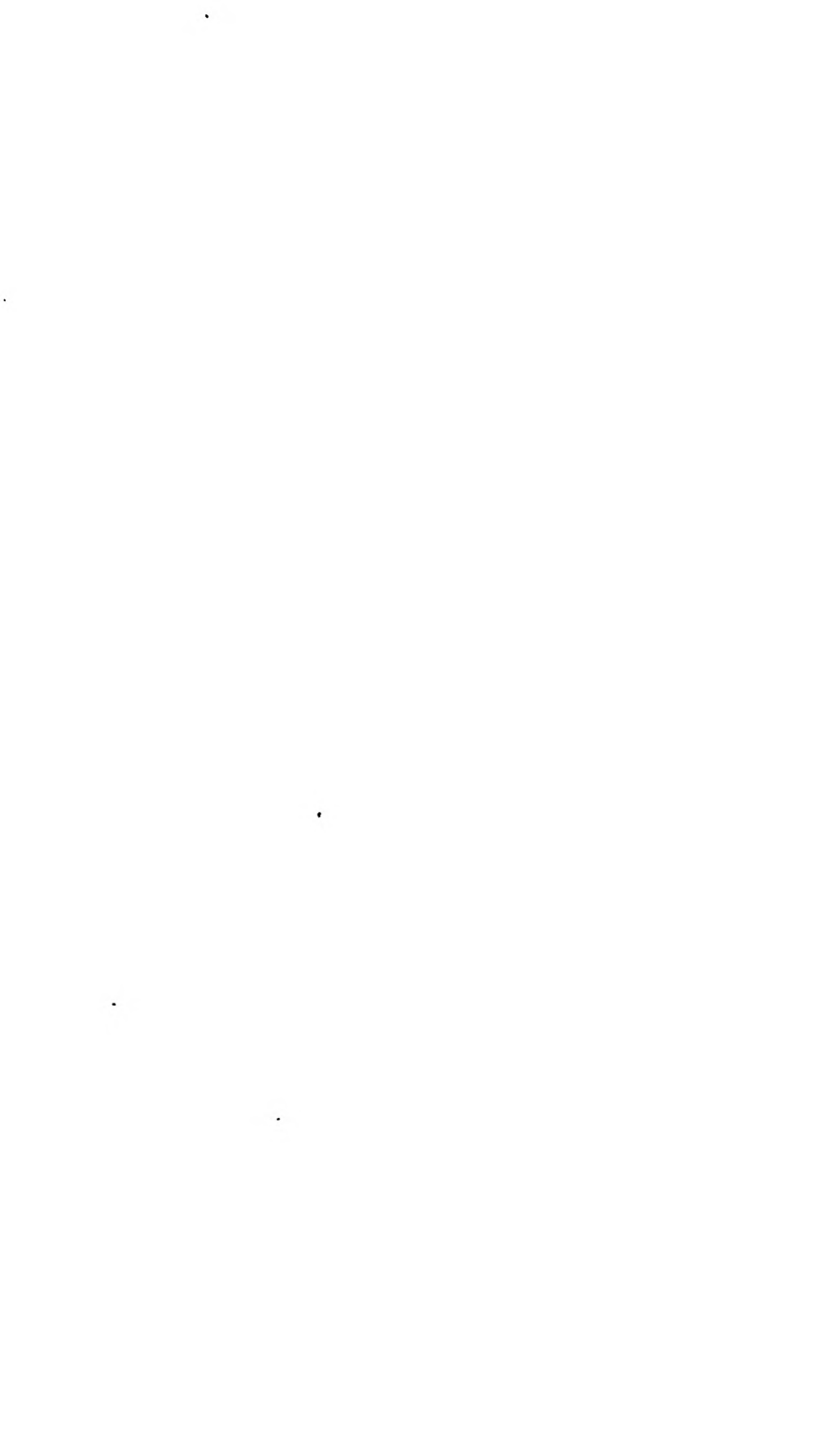
The present illness began in 1895. It had been characterized by attacks, at variable intervals, in which the symptoms were similar to those which had been present during the eight months prior to his consultation, January, 1921. They were as follows: bloating, belching, regurgitation and dull aching pain either in the epigastrium or across the midabdomen. The pain had become severe enough to make the patient very uncomfortable much of the time. It occurred at variable intervals, day or night, and was without relation to food. It was relieved by taking soda or hot water. The appetite was good. There had

been no vomiting, no hematemesis, and no bloody or tarry stools.

The physical examination was essentially negative. Barium x-ray studies of the gastro-intestinal tract, including examination of the colon by a barium enema, showed nothing abnormal. The Wassermann reaction in the blood-serum was negative. The usual clinical laboratory examinations of the blood, urine, and stools showed nothing abnormal.

The patient was placed on a liberal, general diet. All cathartic drugs, including the use of oils, were stopped. The patient was instructed to give himself an enema (from 250 to 500 c.c. of water) every third night. After two weeks the patient's bowels had regulated themselves; he was entirely free from symptoms and still remains so.

The practicability of the plan of therapy which has been outlined is shown by the fact that it is unnecessary for patients to curtail business activities except in occasional cases, and in these for not more than a few weeks. Although the treatment is applicable to most patients with chronic functional gastro-intestinal disturbances, there are a certain number who do not fall into the groups here described; but may be classified in a miscellaneous group. Because of the number and varieties of factors entering into the description of this group, it will not be discussed.



CLINIC OF DR. SAMUEL A. LEVINE

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RAPID HEART ACTION¹

WE are to discuss today the clinical recognition and management of conditions associated with rapid heart action.² In most patients having a very rapid heart it is possible to make a proper diagnosis of the disturbance with a high degree of accuracy at the bedside, using only those means that all of us clinicians have with us at all times. It does not generally necessitate any special apparatus or graphic methods.

A patient may come in complaining of attacks of palpitation. Of first importance is a careful history of the attack. Do they start suddenly and do they end suddenly? Or does the condition gradually develop and gradually die out? These points are of great aid in diagnosis. We are all familiar with the fact that under certain nervous influences the heart may become rapid and pound heavily. But under such conditions the heart rate does not suddenly in one beat jump from normal to 150 or so; it slowly rises and maintains its rapid rate for a variable length of time, and as the nervous excitement abates the heart rate slowly returns to normal. On the other hand, there are times when the patient is clearly aware of the sudden change in rate, and he might say that the palpitation came instantaneously, lasted for one or many hours, and then ended with a sudden thump. This sort of an upset is due to an entirely dif-

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²The very rare forms of tachycardia—*i. e.*, ventricular tachycardia, paroxysmal auricular flutter—are not taken up because of their great infrequency, and because it is impossible to diagnose them without special graphic means.

ferent mechanism, has a different significance, and requires different treatment.

In some instances the diagnosis will have to rest entirely on the history, because the attacks are of such short duration that when the physician examines the patient the attack is over and a normal heart mechanism is found. Here you can readily see that the history has to be taken carefully, with full details as to its onset and ending. It is of considerable importance to enquire whether the termination of the attack is associated with vomiting or any other symptom that might be related in any way to a possible stimulation of the vagus nerve.

On the other hand, when you are first called to see the patient the heart may then be rapid. The past history again will be of great aid in diagnosis, but if the history is not convincing, you will have to depend on the results of physical examination. A rapid heart may be associated with certain well-known conditions. We are all aware of the acceleration accompanying exertion, fright and other emotions, hyperthyroidism, and infections. If there is a high fever such as one gets in pneumonia we may expect occasionally a rate of 140 to 160, but when the rate is over 150 the possibility of an abnormal tachycardia rather than an ordinary acceleration is to be considered. This would surely be true if the rate were in the vicinity of 200. Occasionally the heart rate is extremely rapid in hyperthyroidism, and again the same differentiation needs to be considered. How are we to tell whether an abnormal tachycardia is present or whether the heart's rhythm is normal but rapid? The first procedure is to determine whether the rhythm of the heart as heard over the precordium is perfectly regular. You must remember that when the rate is extremely rapid, around 180 to 200, it may be irregular and yet appear quite regular for variable lengths of time. For this reason it will be necessary to listen carefully for several minutes at a time. If the rhythm is perfectly regular there will be absolutely no disturbance in the regular repetition of the heart cycles. In fact, in the conditions of this kind (called paroxysmal auricular tachycardia) the length of individual heart cycles will not vary even $\frac{1}{100}$ second. Should

there be even very slight difference you can be certain that the heart is not in cardiac arrest.

A further simple procedure for diagnosis is making a count of the heart-beats by palpating this in five or ten full sixty seconds' period, taking the number of beats whatever. If this is repeated in several cases of paroxysmal tachycardia the rate will be found to be the same in the two counts, or certainly within two or three beats of each other. This slight variation can be accounted for by the fact that the heart-beat at the point where the second hand of the watch is at the beginning of the minute to be counted, and by the fact that the final heart-beat at the point where the minute count ends. On the other hand, if the rhythm is even slightly irregular the counts are apt to vary more, even five to ten beats. Cases taken up shortly will illustrate this procedure.

The counting of the radial pulse also throws some light on the diagnosis. When the heart's rate is rapid it is difficult to count the pulse, although it may be very easy to count the apex-beat. However, when it is perfectly apparent that the radial count is considerably less than the apex count, you are apt to be dealing with auricular fibrillation or delirium cordis. Here the rhythm as determined by ausculting the apex will be found irregular, although the irregularity may be only very slight because of the great rapidity. You must not forget that when the heart is beating very rapidly and regularly, palpating the radial pulse may give a wrong impression as to the heart's action. During certain phases of respiration the volume of the pulse may diminish or the pulse may entirely disappear. This would lead one to think that the heart is beating irregularly because some of the beats are apparently missed. You can readily see that when the radial pulse is apparently irregular the rhythm of the heart itself may either be regular or irregular. It is, therefore, always most important to determine the rhythm of the heart by auscultation over the precordium.

By these steps we are enabled to make a clinical diagnosis of

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ferent man of the heart and the type of tachycardia in the great
ferent ty of cases. If the apex rate is perfectly regular and

In, around 180 to 200, and does not vary more than two
the is on repeated counts, even though the radial pulse may
when irregular, we are dealing in most instances with *paroxysmal*
auricular tachycardia. This is a condition in which some part of
the auricular wall has become irritable and has temporarily
taken over the function of pace-maker of the heart. On the
other hand, if the heart rate is rapid and slightly irregular and
the repeated apex counts differ appreciably (five beats or so),
and particularly if the radial count is a great deal lower than the
apex count (pulse deficit), the condition is one of *auricular*
fibrillation (perpetual arrhythmia or delirium cordis).

The treatment of the two conditions differs decidedly.
There is no specific drug therapy for paroxysmal tachycardia.
Various means are employed in the attempt to stimulate the
vagus nerves, such as drinking ice-cold water, inducing vomit-
ing, ipecac, having the patient's head low as compared to the
rest of the body, holding a deep breath, or direct stimulation of
the vagus nerve by pressure over the carotid artery, or by
pressing the eyeballs. In various cases one or the other of these
means have at some time proved effective. From my own
experience, in more than one-half of the patients, one of the
three last mentioned procedures has ended the attack. The
simplest method is to have the patient take a deep breath and
hold it as long as possible; this will frequently bring the attack
to an end. In others this is not effective. Here you should try
the effect of direct vagal pressure. This is done by compressing
the carotid artery on one side or the other with the fingers of
one hand, giving support to the pressure by placing the other
hand behind the patient's neck. The carotid artery must be
completely obliterated. Pressure is exerted for five to ten sec-
onds, and frequently if you listen to the heart simultaneously you
will hear the tachycardia stop, followed by a pause, then pos-
sibly one or two extra beats, and then the normal slow heart
action will begin. The procedure may be slightly uncomfort-
able for the patient, but is not painful; you should try first one

side, then the other, and repeat the procedure. You may not be successful the first time and yet be able to end the attack a minute later.

The final method that I have found of use in rare instances is direct pressure on the eyeball. This sends an impulse up the fifth cranial nerve and down the tenth. It is called the oculo-cardiac reflex, and in the normal person the heart may be considerably slowed in this way. The procedure is rather painful and should not be resorted to unless circumstances warrant the discomfort or unless the patient is unconscious, as happens if a patient goes into an attack while under an anesthetic for a surgical operation. Occasionally ocular pressure will be successful in ending an attack when all other methods fail.

The treatment for the other form of rapid heart action—*i. e.*, auricular fibrillation—is digitalis. You must remember that digitalis will have no effect whatever on the first condition described (paroxysmal tachycardia), but will prove very beneficial for the other. In patients with extremely rapid and irregular heart rate a fairly large dose of digitalis can be given, especially if a quick result is desired. The ventricular rate can be slowed frequently to the normal in a few days, or even in six to twelve hours. The abnormal rhythm is not changed essentially by digitalis, but the drug merely diminishes the number of impulses that reach the ventricle. The paroxysm of auricular fibrillation may continue for hours or days and then return to the normal rhythm, or it may become permanent. In paroxysmal auricular tachycardia we have just said that vagal pressure not only slowed the heart, but ended the abnormal attack. In fact, vagal stimulation is either completely effective in ending the attack or has no influence whatever on it. Digitalis, on the other hand, does not necessarily end the attack, but almost always slows the ventricular rate if the condition is auricular fibrillation. Vagal pressure might produce a slowing of the ventricular rate, but will never end such an attack. You see how opposite are the effects of vagal stimulation and digitalis in these conditions. The cases to be discussed take up these various points and illustrate how the diagnosis is

made without any special instrumental aid and how to manage the conditions.

Case I.—This patient (Med. No. 12,207) I want to discuss is a seamstress twenty-four years old who came into the hospital complaining of heart spells. The family history is unimportant and she is not married. In childhood she had measles, mumps, whooping-cough, and frequent sore throats. At the age of ten she had acute rheumatic fever and was sick for one month. About one year after the rheumatic fever, while jumping rope, she suddenly was taken with a queer sensation in her throat and her heart seemed to be thumping vigorously and rapidly. She felt faint and had to go to bed, where she remained two weeks. At the end of this time she vomited, and the attack ended as suddenly as it had begun. Since then she has had about two attacks a year, lasting several hours and always ending after a vomiting spell, which she would not voluntarily induce. The attacks she thinks were associated with excitement, exertion, or some dietary indiscretion. In recent years they have been of shorter duration, lasting about twelve hours; but have been coming more frequently and always terminated by a vomiting spell. She gradually noticed slight increasing dyspnea, but her general health was pretty fair between attacks.

On physical examination the patient appeared to be a rather frail young woman lying comfortably in bed. General examination was negative except for the heart. The heart was found normal in size. The first sound at the apex was snapping in quality and distinctly louder than normal. It was preceded by a short presystolic rumble, which ended in the sharp first sound. The rhythm was regular and rapid, 120 to the minute. Two days later, while resting quietly in bed, her heart suddenly began to thump. At this time an accurate apical count was made and found to be 233; this was repeated in ten minutes, and again found to be 233. The diagnosis of paroxysmal auricular tachycardia in a patient with mitral stenosis was perfectly apparent. This was confirmed by electrocardiogram tracings. It was to be expected that this type of case should respond to some form of vagal stimulation, especially as her attacks in the

past always ended after a vomiting spell. With this in mind several attempts at vagal pressure were made, trying the left and the right sides alternately, without success. Then she was told to take a deep breath and hold it as long as she could, but that failed to stop the attack. Just before giving up hopes of ending the attack by any of these means, left vagal pressure was tried again, and the heart promptly and suddenly slowed down to its normal rate. Fortunately, we obtained an electrocardiogram tracing of this transition (Fig. 196) which gives a typical picture of how these attacks end. You can see the rapid regular heart rate racing along, and then suddenly there is

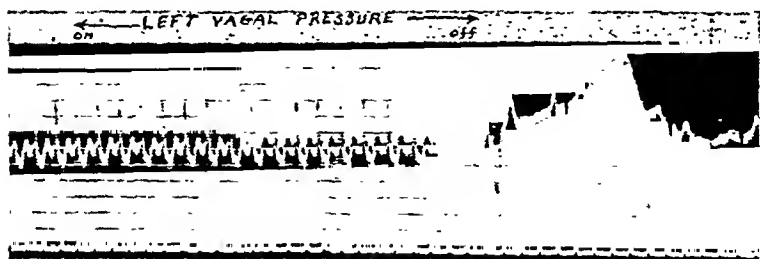


Fig. 196.—Case I. The electrocardiogram shows how left vagal pressure ended an attack of paroxysmal auricular tachycardia. The heart rate at the beginning of the tracing is 233, then there is a sudden pause, an abnormal beat (an extrasystole), followed by the normal rhythm. The irregular base line is due to muscular movement of the patient. Timer below in one-fifth second.

a pause followed by a peculiar heart-beat (an extrasystole), and finally the normal slow heart action is taken up. The attack was thus ended by vagal pressure without causing any discomfort to the patient.

You must bear in mind that arresting any such attack of tachycardia in itself has no influence on the subsequent recurrence of similar attacks. As most of the patients who have such disturbances are not very materially injured by their attacks, it generally does not matter much if they are ended by what we do or not, because they are self-limited and eventually end of themselves. It is possibly true that if attacks are al-

lowed to continue for a long time they become more stubborn and subsequent attacks may be arrested with greater difficulty. In this patient the first attack lasted two weeks, and very likely the discomfort and confinement to bed for such a long time might have been prevented. In other cases, however, the attack may supervene on a patient already suffering from considerable cardiac failure with organic heart disease. In such instances it is of greater importance to stop the paroxysm and release the heart from the additional strain of the rapid rate. Furthermore, such attacks may occur while patients are under an anesthetic for a surgical operation. I have had the opportunity of seeing 3 such patients. In 2 of them the circulation did not seem to be embarrassed very much and the attacks were ended only after the operation was finished. In a third, however, the attack began in the early stages of anesthetization, before the operation had actually begun. The heart rate suddenly jumped to 216, the patient became markedly cyanosed, pulseless, and stopped breathing. It seemed imperative to restore the normal rhythm if possible. Pressure over the left carotid artery for several seconds promptly accomplished this, the rate fell to around 100, and the general condition of the patient returned to normal. The patient was subsequently operated on and a gall-bladder full of stones removed.

Case II.—The following patient illustrates how attacks of tachycardia may arise as a complication during a surgical operation. An engineer of forty-six came into the hospital complaining of a lump in the neck. The family history was unessential. At the age of sixteen he had gonorrhea and also a chancre, but did not know whether it was hard or soft. He received no special treatment. He had been a fairly heavy drinker for many years. Twenty-five years ago a mass, the size of an orange, gradually developed on the right side of his neck below the angle of the jaw. This mass was then removed, and he had no trouble until two years ago, when a small lump appeared below the scar of the previous operation. Four months ago this was removed, but he thinks the surgeon "left a little in the neck." He entered the hospital because the lump was

growing larger and becoming sore. Physical examination was entirely negative except for the old scar and a mass in the neck, the size of a plum. The heart was definitely enlarged, the left border was 2 cm. to the left of the nipple line. The sounds were normal, the rhythm was slow and regular, and there were no murmurs. The Wassermann reaction was negative. It was decided to operate for recurrent carcinoma of the glands of the neck.

The patient had no particular difficulty with the anesthetic and the dissection of glands of the neck did not seem to cause any

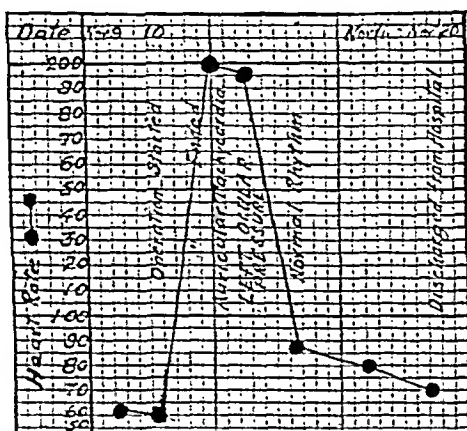


Fig. 197.—Case II. Chart shows how left ocular pressure ended an attack of paroxysmal tachycardia in a patient still under ether for a surgical operation. The heart rate fell from over 190 to under 90.

undue disturbance in the patient, when, just as the operation was nearly at an end, the heart-rate suddenly jumped to about 200. The operation was quickly finished, and when I saw him he was still under the influence of the ether anesthetic. The heart-rate was perfectly regular—189 to the minute. The general condition of the patient seemed to be fairly satisfactory, although the pulse was very thready. The condition was diagnosed paroxysmal auricular tachycardia and was confirmed by electrocardiograms. Repeated attempts to stop the attack by compressing the right and left carotid arteries proved unsuc-

cessful. Inasmuch as it was not known how long the attack might last and how badly it might affect the surgical convalescence, and, moreover, because the patient was still unconscious it was thought justifiable to try the effect of pressure over the eyeballs. This proved effective, for pressing on the left eyeball suddenly brought the attack to an end (Fig. 197) and the heart-rate dropped to about 90. In this case there was no evidence that there had ever been any previous attack of tachycardia and the patient never had any subsequent attacks during the three years that he lived. He finally died of recurrent carcinoma.

Case III.—The following case that I wish to discuss presents a different problem. Here during surgical convalescence the patient's heart-rate suddenly became very rapid, but irregular. *In this condition the various procedures that stimulate the vagus nerves are of no help; but, on the other hand, as we will shortly see, digitalis controls the heart condition in an admirable way.* This patient is a single woman forty-nine years old, whose family history and past history were unimportant except for occasional attacks of palpitation accompanied by some shortness of breath. Five years ago she was operated on for appendicitis and a fecal fistula developed following the operation. About one year later she was operated on again and the fecal fistula successfully closed. She remained in good health except for an occasional attack of palpitation. She noticed that there was developing a protrusion at the site of her old abdominal scar. She was operated on for a ventral hernia and nothing of unusual interest occurred during the operation. The patient was doing satisfactorily, when, on the second day following the operation, she suddenly became worse. The heart-rate became very rapid and absolutely irregular—145 at the apex and only 100 at the wrist. The diagnosis of auricular fibrillation was made because of the gross arrhythmia in force and rate of the heart-beats and the marked pulse deficit. It was considered paroxysmal because she gave a history of previous attacks of palpitation, and those were thought to be probably of the same nature. One could not be certain whether

this particular attack was to be transient or permanent, as most of the patients with auricular fibrillation eventually settle down into the permanent form of the arrhythmia. She was given 0.5 gram of digitalis leaves in one dose, and after about sixteen hours the attack was over, the heart-rate was regular, and the pulse was 70 to the minute (Fig. 198). We were still in doubt as to whether the patient was going to have any more attacks, and therefore gave her no more digitalis. Two days later, however, she had another attack that was not so bad. The apex-rate only rose to 127, while the pulse was 93. At this point it was decided to get the heart fairly well digitalized in prepara-

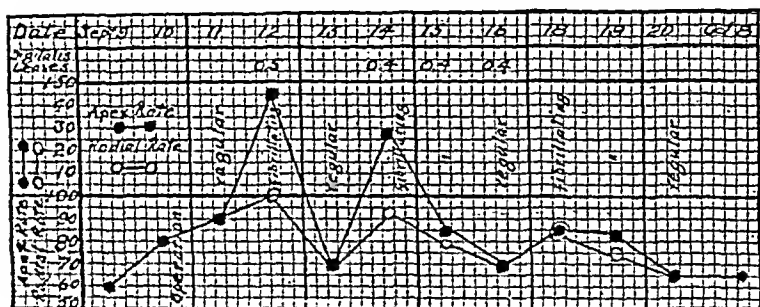


Fig. 198.—Case III. Chart shows paroxysmal auricular fibrillation during surgical convalescence and how digitalis therapy controlled the heart rate. Apex and radial rates are indicated.

tion for subsequent attacks, and so she was given 0.4 gram of digitalis daily. This second attack lasted about twelve hours before the normal heart mechanism returned. The interesting thing is that four days later she had a third attack, but this time was absolutely unaware of it. The heart-rate at the apex was found to be 84 and the same number could be counted at the wrist, *i. e.*, there was no pulse deficit and the rate was normal. The only change was in the rhythm, for the previously regular heart had again become absolutely irregular, only this time, because the heart had been prepared for the attack by sufficient digitalis medication, no change took place in the rate or in the subjective symptoms of the patient. Quite evidently the em-

barrassment in such patients is from the rapidity of the heart and the resulting impaired circulation, and not from the fact that it is irregular in rhythm.

The development of paroxysmal auricular fibrillation (transient absolute arrhythmia) is not an uncommon event during surgical convalescence, and the case just discussed illustrates the beneficial results to be obtained by the proper use of digitalis. When the attack results in an extremely rapid heart-rate it is necessary to distinguish the condition from paroxysmal auricular tachycardia. The differential points taken up earlier in the discussion will enable you to make the diagnosis in the great majority of cases. Such a differentiation is absolutely necessary because digitalis has no beneficial effect whatever on the one and is extremely helpful in the other, while vagal stimulation may end the attacks of tachycardia and have no beneficial effect on fibrillation.

Case IV.—This patient (Med. No. 15,716) presented a problem that concerns us in this discussion. She is a saleswoman thirty-seven years old, and came in complaining of pain in the stomach. Her family history is negative except that her mother has a bad heart. She was married, but has become divorced. She never was pregnant. She had measles, chicken-pox, diphtheria, and mumps as a child. Three years ago she was sick for three weeks with influenza. For many years has had acute tonsillitis every winter, which always confined her to bed for a week or so. She had some dyspnea on exertion and occasional palpitation. This in no way actually interfered with her routine work. Eight years ago she had an attack of pain in the right upper quadrant requiring morphin; there was jaundice at this time. The menstrual history is negative. She has lost no weight, is not troubled with cough, and has never noticed swelling of the feet.

One month ago she began to feel feverish and chilly and had a sore throat. Her doctor called it tonsillitis. She then developed nausea, epigastric distress, and pain, with occasional vomiting spells. The pain gradually got worse. These abdominal symptoms brought her to the hospital. She says that there

has been some trouble with her heart for about ten years because doctors have always been curious about her condition.

General physical examination when she first came to the hospital was negative except for the findings in the heart. The apex was diffuse, but felt in the fifth space outside the nipple line. A short thrill was felt, but the actual timing was impossible because of the great rapidity. The left border was 16 cm. to the left of the midsternal line in the fifth space and the right border 2.5 cm. to the right. On auscultation the heart-rate was found to be extremely rapid and at times perfectly regular, but on careful examination slight irregularities could be definitely detected. A full minute count of the apex-beat was 178, and five minutes later was 171. The radial count at this time was 140. The first sound at the apex was accentuated and was followed by a systolic murmur. There seemed to be a murmur in diastole, but the exact timing of it was very doubtful because of the rapid heart-rate.

As far as the rhythm of the heart was concerned, the two conditions to be considered were paroxysmal auricular tachycardia and auricular fibrillation. A striking point in the clinical picture was the fact that the patient had very little dyspnea, no edema of the extremities, or congestion of the lungs. The patient could lie perfectly flat in bed with no discomfort except the abdominal distress. This sort of picture frequently goes with paroxysmal tachycardia, and made us all think of this possibility. However, there were several points which indicated that the diagnosis was auricular fibrillation. First, the rate was not absolutely regular, and two successive counts varied by seven beats. Second, there was a considerable pulse deficit, the radial pulse was 140, while the apical count was 178. This proved to be the correct diagnosis as shown by the electrocardiograms that were immediately taken.

As I have indicated before, such a condition should respond readily to digitalis treatment. It was learned that her doctor had given her some tincture of digitalis; it was thought from the extremely rapid rate that she had not had enough digitalis, and so 0.9 gram of powdered digitalis leaves (equivalent to 9 c.c. of

a standardized tincture) was given immediately in one dose, and several hours later an additional 0.2 gram was given. A most striking result was obtained, for the next morning the heart-rate at the apex was 70 and the rate at the wrist was 66 (Fig. 199). There is no other condition in which such a marked effect on the heart can be produced by any form of medication, and also there is no other drug that will produce such an effect in this condition except digitalis or one of the allied preparations. Digitalis is as specific in reducing the heart-rate in auricular

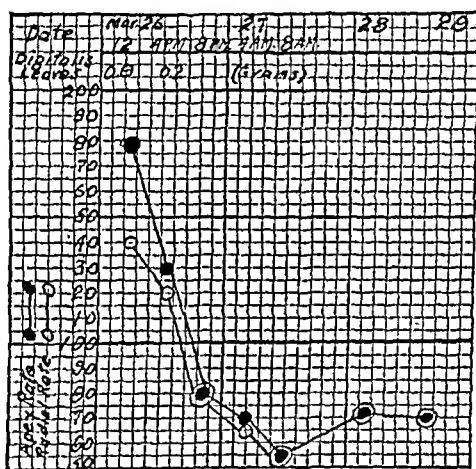


Fig. 199.—Case IV. Chart shows the quick effect of a large dose of digitalis on the rapid heart rate associated with auricular fibrillation. The apex rate fell from 178 to 55 in twenty hours.

fibrillation as quinin for malaria. The patient's general condition improved, and although she had a flare-up of rheumatic fever, has done very well. The auricular fibrillation in this case is permanent and not transient, and probably will continue indefinitely, though the ventricular rate can be kept slow by the use of digitalis. On the first day when the heart-rate was 178 vagal stimulation might slow the heart for a few seconds, but could not stop the rapid rate as happened in the first two cases considered.

Summary.—Two cases of paroxysmal auricular tachycardia and two cases of auricular fibrillation are discussed (one transient and one permanent). The methods of diagnosis are considered, and it is shown how the conditions may be distinguished by very simple means without any special apparatus. It is explained how vagal stimulation may end the attacks of the former and how digitalis will control the condition in the latter. Their occurrence during or after a surgical operation is illustrated by two of the cases.

CLINIC OF DR. ELLIOTT P. JOSLIN

NEW ENGLAND DEACONESS HOSPITAL

PRACTICAL LESSONS FOR PHYSICIANS AND PATIENTS IN DIABETES

Pliability of the Diet in Diabetes as Well as in Health; the Dangers of Fat in the Diabetic Diet; the Critical Period of Hypoglycemia in Undernutrition; Renal Glycosuria.

Introduction.—The pliability of the diet in diabetes as well as in health, the danger of fat to the diabetic, the critical period of hypoglycemia in undernutrition, and renal glycosuria are four topics which continue to furnish practical lessons for patients and physicians alike.

1. The Pliability of the Diet.—At the recent meeting of the Inter-Urban Club in New Haven Professor Mendel emphasized the extraordinary adaptability of the diet as shown by recent experiments. He described how animals can be raised upon protein and salts without either carbohydrate or fat, provided the fat-soluble vitamin is supplied, and also called attention to the possibility of the fats being burned in the flame of amino-acids as well as in that of carbohydrate. "Pliability of the diet" is a term peculiarly pertinent to diabetes because the dietetic treatment of this disease rests upon the possibility of extreme deviations from the proportion of carbohydrate, protein, and fat customary in the diet of healthy individuals. The pliability, therefore, is theoretically most advantageous, and, in fact, is so great that it makes good treatment of early cases of diabetes feasible in manifold ways. Thus, early or mild cases of diabetes will become sugar free with restriction of carbohydrate, restriction of fat, or restriction of protein, and all of these methods

have been employed with varying success. It is to the credit of F. M. Allen, however, that the basic principle underlying all these methods has been shown to be undernutrition. Such is the pliability of the diet that with this provision almost any old diet will produce fairly good results in early cases of diabetes.

On the other hand, despite these advantages this very quality brings with it almost still greater disadvantages. Success, or apparent success, is attained in so many ways that the dangers resulting from the persistent employment of this or that method are frequently overlooked. This is due to the fact that the harmful effects of any one diet seldom show immediately, and the long interval before they exert themselves is often so great that they escape attention, partly because of loss of perspective on the part of the physician, partly because the patient has passed from observation. Permanent success in the dietetic treatment of diabetes can be obtained only by the continual observation of patients throughout the comparatively long and increasing period which constitutes the diabetic's span of life. During this interval faithfully kept records with frequent summaries will alone disclose the better methods of treatment.

Criticism of special, even bizarre, methods of dietetic treatment must be employed with only the greatest caution because of the pliability of the diet. Arbitrary statements are seldom justified, and are too often made, only to be retracted. It is very necessary for both physicians and patients to bear this in mind, because otherwise the good points of treatment prescribed in one locality may receive undeserved discredit in another. In a recent compilation of all the studies carried out at the Nutrition Laboratory of the Carnegie Institution between 1908 and 1917 the writer has found it desirable to separate the data by the arbitrary date, June, 1914, at which time the method of undernutrition was introduced. The two epochs of treatment differ so widely that if those methods in general use prior to 1914 were adopted now, it would almost seem like malpractice, whereas, prior to 1914, the formulation of a plan to treat patients as is now commonly in vogue would have appeared like an unjustifiable experiment. No wonder the

practitioner is bewildered by the changing advice which his diabetics receive from year to year from those supposed to know the best methods.

2. **The Dangers of Fat in the Diabetic Diet.**—Obesity is coincident with the onset of diabetes in 3 cases out of 4, and in some decades of life in 39 cases out of 40. So great is the importance of fat in the causation of this disease! Recognition of this etiologic factor should lead to a reduction in the number of diabetics. Each diabetic should serve his fellowmen by disseminating this doctrine. For each case in which undernutrition is helpful in treatment who knows but that earlier application of the same doctrine may prevent 10 or 100? How much easier it is to prevent than treat!

The danger of fat in the early days of diabetic treatment is now generally appreciated. It is not many years ago that so soon as the diagnosis was made the fat and protein in the diet were increased and carbohydrate restricted. Such a diet, suddenly begun and energetically pushed, frequently led to the death of the patient in diabetic coma within a few days. Even the pliability of the diet was not great enough to prevent fatalities which today are recorded as unnecessary. It was this great increase in the quantity of fat and corresponding decrease in the quantity of carbohydrate which made the first year of treatment the diabetic's danger zone.

The prolonged use of large quantities of fat in proportion to small quantities of carbohydrate is less thoroughly recognized. It is my belief that the further the diabetic's diet departs from the normal proportions of carbohydrate 4, fat 1, in order to attain a sugar-free urine and blood-sugar of normal value, not only the more serious is the case, but the less the chance for that patient to improve in tolerance for carbohydrate. When the total caloric value of the diet is low a comparatively high proportion of fat often appears to be harmless, though this is said with great reserve; but when the diet is fairly liberal and the proportion of carbohydrate to fat falls below 1 to 5 in contradistinction to the normal proportion of 4 of carbohydrate to 1 of fat, this inverted proportion almost invariably results in harm.

aspect of the patient has changed for the better. It is hoped and confidently expected that this patient, like the former just cited, will eventually regain still more tolerance. Had it not been for the excessive use of fat for seventy days there appears to be no reason why this patient should have lost so much tolerance. Until these 2 cases I have recently been inclined to believe that when a diabetic adopted a high fat low carbohydrate diet, he was passing through a portal above which might well have been inscribed "Abandon hope all ye who enter here."

3. The Critical Period of Hypoglycemia in Undernutrition.—The discovery of the presence of hypoglycemia during the course of treatment by undernutrition is a danger signal of the first importance. Case No. 1085, a frail woman of thirty-four years, with a history of diabetes of seven months' duration, became sugar free with great difficulty, despite fasting and a low diet. After four months the sugar in the blood decreased from over 0.50 to 0.10 per cent. coincident with a fall in weight from 88 to 61 pounds, of which the last 10 pounds were lost between November 3 and 10, 1916. No subsequent blood-sugar determination was made, but inasmuch as a few days later, without change in treatment or in general condition at her home, she died without pain or coma, there is little doubt that hypoglycemia was present.

Rather similarly, Case No. 1831, a man with onset of diabetes April, 1917, at the age of thirty-eight years and seven months, entered the hospital May 5, 1920. The details of the course of treatment with laboratory findings are shown in Table I. It will be observed that acidosis was present, sugar in the urine amounted to 2.4 per cent., and in the blood to 0.36 per cent. After four days of undernutrition, during which the total calories consumed amounted to less than 900, followed by two days of fasting, the patient failed to become sugar free and the blood-sugar remained 0.29 per cent. Upon resumption of 14 to 35 grams of protein per day and 3 to 8 grams of fat the blood-sugar dropped to 0.11 per cent. On the next day, despite a slight increase in protein and fat and 2 grams of carbohydrate, the

blood-sugar was 0.05 per cent. This unusually low value was assumed to be erroneous and, unfortunately, not reported to the physician. Upon the following morning the patient became irrational, disoriented, but an hour afterward again apparently normal, and was able to sit up and even walked around. Physical examination was negative. The following morning he could not be roused, coma gradually deepened, though unassociated with acidosis, and death occurred in a few hours. The blood-sugar was 0.04 per cent. No marked loss of weight was observed in this patient, but, fortunately, quantitative examinations of the nitrogen in the urine were made and showed an average excretion of 16.9 grams during five days and 19.6 grams during four of the following five days preceding death.

Experience with these two individuals made it possible to forestall a similar outcome with Case No. 2079. This man developed diabetes in September, 1919, at the age of twenty-nine years and nine months, and came for treatment on February 5, 1921, weighing 119 pounds after a loss of 66 pounds below his maximum weight. Acidosis was severe, sugar in the urine 5.8 per cent., and blood-sugar 0.27 per cent., and even after thirty days of treatment the blood-sugar was 0.23 per cent. Yet two days later the patient became sugar free, and within a week the blood-sugar was 0.12 per cent., and on the forty-third day 0.09 per cent. This premonitory fall in blood-sugar being noticed, the diet was at once changed to carbohydrate 19 grams, protein 59 grams, fat 62 grams. Despite the fact that this patient had required so long to become sugar free, steady additions of carbohydrate were made to the diet until on the forty-ninth day from admission the total carbohydrate was 68 grams, the protein 71 grams, the fat 66 grams, and the blood-sugar was 0.05 per cent. Even one hour after a meal two days later, when the carbohydrate was 86 grams, the blood-sugar was 0.10 per cent. The patient was then discharged with carbohydrate 82 grams, protein 74 grams, fat 66 grams, calories 1234, weight 92 pounds, in contrast to a weight of approximately 110 pounds on the first day of treatment. Two weeks later the report comes that his blood-sugar is 0.10 per cent., and that he has

TABLE I

Date.	Volume, c c.	Alb.	Diacetic acid.	Sodium chlorid.	Nitro- gen, gm.	Sugar in urine.	Diet in grams.				Naked weight, pounds.	Non- protein nitrogen.	Blood's blood fat, per cent.	Blood- sugar, per cent.	Alveo- lar air, CO ₂ , mm. Hg.
							Carbo- hydrate.	Protein.	Fat.	Calories.					
1920															
May 5	1600	...	++	2.3	23	15	179	93	30
5-6	3000	0	++	2.4	64	33	3	3	388	93	30
6-7	2000		+	1.8	36	27	0	0	252	96	26.1	0.36	
7-8	3300		0	1.7	15	5	0	0	80	95	
8-9	3300		0	0.7	0	0	0	0	0	96	
9-10	3800		0	6.7	16.9	0.4	0	0	0	0	0	95	35
10-11	2800		0	6.1	16.9	0.4	0	0	0	0	0	94	
11-12	4200	0	0	6.1	16.9	0.2	0	0	0	0	0	94	0.29
12-13 ²	4600		0	6.1	16.9	0.1	0	14	3	3	83	95	
13-14	3800		0	6.1	16.9	0	0	21	5	8	129	94	
14-15	1600		0	6.1	16.9	0	0	35	10	212	246	96	0.11
15-16	3800		0	...	19.6	0	1	43	16	332	422	91	0.05
16-17	4700		0	...	19.6	0	2	50	22	488	1.10	
17-18	4600		0	...	19.6	0	4	57	28	
18-19	2700	0	0	...	19.6	0	13	46	Died	1.55 P. M.	0.04
19															

¹ Aliquot values.² NH₃ 0.5 m.

preserved his tolerance. Such a gain in tolerance from such a critical state has not before come to my attention.

4. Renal Glycosuria.—The subject of renal glycosuria has received much attention in the last few years. In general, the criticism raised against the cases reported has been based upon the short period during which patients have been under observation. This criticism does not apply to Case No. 2165, about to be called to your attention. He developed glycosuria at the age of twelve years in June, 1894, and first consulted me April 19, 1921. During these twenty-seven years sugar has been present in the urine at all examinations save one. During the first ten years of treatment, so far as he is aware, the sugar in the urine did not fall below 3 per cent. On physical examination he appears well developed, height 5 feet, 10 inches with shoes, weight 151 pounds dressed, in contrast to his highest weight of 155 pounds, reflexes normal, teeth good, no acetone odor, blood-pressure 130/80, pulse 80, no arteriosclerosis, heart and lungs normal, liver edge felt 1 to 2 cm. below the costal margin, no enlargement of spleen or kidneys. No edema. The Wassermann reaction was negative.

Glycosuria was originally discovered when the patient was undergoing treatment for asthma. During these twenty-seven years he has led a normal life, and at present occupies an important position as an electric engineer. For the first six weeks of treatment, at the age of twelve, the diet consisted of milk and eggs exclusively. This was followed by a diet free from potatoes and white bread, but while in college he ate a full diet, except for the omission of sugar and desserts. As a rule the percentage of sugar in the urine has ranged between 1 and 4, and has been reported to have been as high as 10 per cent. Last autumn, during a conference at his office, he became faint, went home, rested a few days, restricted his diet, and a single specimen of urine of specific gravity 1042 was said to be sugar free, but a few weeks later sugar was reported to be between 8 and 10 per cent.

The percentage of sugar in the twenty-four-hour quantities of urine examined here ranged between 2.5 and 2.9 per cent., but in

the course of a two-hour renal test the range was somewhat greater, namely, 2.3 to 4.2 per cent., and the total quantity of urinary sugar for the two days upon which the patient was under observation amounted to 52 and 58 grams respectively. The diet which he selected at the hospital, as comparable to his diet at home, contained carbohydrate 225 grams, protein 100 grams, fat 110 grams. As a matter of fact, he probably took an additional quart of milk when at full work. This would be consistent with the large quantity of nitrogen in the twenty-four-hour quantity of urine, namely, 21.3 grams.

Six estimations of the blood-sugar were made. The blood-sugar on the afternoon of April 19th was 0.10 per cent., the blood-sugar, fasting, April 20th was 0.10 per cent., upon April 21st the fasting blood-sugar was 0.07 per cent., half an hour after breakfast it was 0.10 per cent., one and a half hours after breakfast it was 0.09 per cent., and three and a half hours after breakfast it was 0.10 per cent.

The condition of the kidneys was apparently excellent. There was but the slightest possible trace of albumin, while blood, pus, and casts were absent. The specific gravities of the urine ranged from 1022 to 1042. The percentage of sugar has already been given. The percentage of salt in the urine varied from 0.48 to 0.86. During the day the quantity of urine was 1200 c.c. and at night 950 c.c. The phenolphthalein test showed an excretion of 62 per cent. for the two hours and ten minutes after administration.

Here then is a case in which a boy of twelve shows a large percentage of sugar in the urine which persists during a period of twenty-seven years. At the end of that time the blood-sugar is normal under all conditions, and the patient appears to be in good health. It is notable that the teeth are normal, the arteries normal, the heart normal, and the kidneys normal. There is no evidence of disturbance of vision. A case like the present encourages one to hope that renal glycosuria may yet be proved to be an entity.

CLINIC OF DR. GEORGE R. MINOT

MASSACHUSETTS GENERAL HOSPITAL

TWO CURABLE CASES OF ANEMIA

- I. Chronic Hemolytic Anemia—"the Pernicious Anemia of Pregnancy."
- II. Myxedema with Anemia.

I HAVE two patients to show you today, both of whom have anemia that is curable provided the cause is recognized and proper treatment is carried out.

CASE I

The first patient is a woman twenty-eight years of age, who is eight months pregnant. Her history is as follows:

Family History.—She has given birth to 2 healthy children, two and four years ago. She had no abnormal symptoms or physical signs during these pregnancies. There is no family history of anemia, and her father, mother, brother, and sister are living and well.

Past History.—Ten years ago she had an attack of acute appendicitis and the appendix was removed at that time. Owing to frequent recurrence of colds and mild sore throats, her tonsils and adenoids were removed a year ago. She had measles and chicken-pox as a child, but has had no other diseases. She considers that she always has been well and strong and of a normal color. She denies having had in the past any symptoms referable to any of the systems of the body except as referred to above.

Present Illness.—Early in her present pregnancy she experienced distinctly more nausea than she had in her two previous

ones. At the end of the third month, now five months ago, she noticed she was somewhat pale and realized that she became tired easily. Since then she has grown increasingly weaker. However, up to six weeks ago she felt but slightly weaker than five months ago. During the past six weeks, coincident with the increase of her sensation of feeling "all in," her pallor has become much more marked. She has had some slight dyspnea on exertion, and at such times she has noticed that "her heart beat rapidly." For the past two weeks she has suffered from inability to sleep and from sweating, especially shortly after she got to sleep. She also has noted ill-defined numbness in her hands and feet. These sensations have not been persistently present, and have occurred particularly when she was cold.

Five weeks ago there was a hemorrhage of about 3 ounces from the vagina. A pelvic examination made at that time by her obstetrician did not reveal a placenta prævia or other abnormality. There have been no other symptoms, including no gastro-intestinal symptoms, and none referred to her tongue.

Physical Examination.—The patient appears distinctly pale, and though not of a definite lemon tint, she does appear of a light saffron color, which is more evident upon looking at the trunk than at the face. The scleræ are not yellowish. There has been no elevation of temperature in the past four days, since the patient has been in bed, and the pulse-rate has averaged 100 per minute. The respiration has not been increased. The patient appears bright and cheerful, and states that she feels well provided she remains in bed. The pupils, reflexes, sensation, lymph-nodes, thyroid, teeth, nose, and throat appear normal. The tongue is not atrophied or shiny and appears clean. The lungs are negative to auscultation and percussion. The heart appears normal in all respects except for a soft systolic murmur at the base, which can easily be explained as functional and dependent upon her anemia. The systolic blood-pressure is 120, and the diastolic 80. The abdomen and breasts are characteristic of an eight-month pregnant woman. The edge of the liver can be felt 2 cm. below the costal margin on deep inspiration. It is not tender. The upper border of the liver

is in normal position. The spleen can just be felt on very deep inspiration with the patient on her right side.

Laboratory Examinations.—The *stool* is negative.

The urine shows a trifling amount of albumin, but is otherwise negative.

The Blood.—Hemoglobin, 45 per cent. Red cells, 3,100,000 per cu. mm. Color index, 0.7+. The hematocrit shows 21 per cent. cells and 79 per cent. plasma.

The red cells were studied in fresh preparations vitally stained with brilliant cresyl blue and in fixed Wright stained blood-smears. They are definitely abnormal. They show moderately marked variation in size. The cells average smaller than normal, though one sees numerous cells that are definitely larger than normal, but these are all polychromatophilic cells. There are no large abnormally shaped cells present. The large polychromatophilic cells are round. True microcytes are present, but rare. Cells showing tailing and evidence of fragmentation are occasionally seen, but are not very plentiful. Marked achromia is present. There are, however, some cells about half the size of normal which stain deeply. Such cells probably represent fragmented cells. Abnormality of shape, though present as indicated, is not of a very marked degree. Besides cells showing the more usual abnormal forms and cells showing tailing, one finds numerous long, narrow, round-ended red cells.

The reticulated cells are 16 per cent., while polychromatophilic cells occur as frequently as 3 or 4 to an oil-immersion field. Rarely fine stippling occurs. Besides the reticulated cells, one observes in the vitally stained preparations that the cells take the stain unevenly, so that some cells stain distinctly grayish, in contrast to the greenish color of the majority. True blasts occur; three were found in counting 300 white cells.

The fragility of the red cells to varying strengths of salt solution shows as follows:

	The case.		The control.	
Hemolysis begins.	0.54	per cent. NaCl	0.42	per cent. NaCl
Hemolysis marked . . .	0.44	" "	0.36	" "
Hemolysis complete	0.32	" "	0.30	" "

The serum is yellow and gives a positive Gmelin test. The serum contains a definite excess of bile-pigments as shown by the fact that it must be diluted many more times than normal serum has to be before the yellow color disappears.

In the duodenal contents the bile-pigments were found to be definitely increased above normal.

The platelets are 240,000. This indicates that they occur in normal numbers. Their character is not abnormal.

The coagulation time is normal, and the clot retracts normally. The white cells are 6000 per cu. mm.

The differential count of 200 cells is as follows:

Polynuclear neutrophils.	72 per cent.
Lymphocytes.....	23 "
Large mononuclears.....	3 "
Neutrophilic myelocytes.....	2 "
	<hr/>
	100 "

No polynuclear eosinophil or basophil cells were seen.

The Wassermann reaction is negative.

Discussion of the Case.—The patient's symptoms of weakness, sweating, slight dyspnea, and palpitation can easily be explained as due to the anemia *per se*.

From the appearance of the patient and her history of progressive weakness one might think she had primary pernicious anemia. However, pernicious anemia is rare below the age of thirty, and she has not had any of the special symptoms commonly seen in this disease, namely, a recurring soreness of the tongue or symptoms referable to degeneration of the spinal cord. The numbness in her hands and feet suggests perhaps a disturbance due to degeneration of her spinal cord. This sensation has not been persistent or associated with tingling or with ataxia, as is typical in a case of pernicious anemia. It is very common for individuals with anemia from any cause to have temporary numbness in the hands and feet due to an insufficient amount of oxygen-carrying material, namely, hemoglobin. It is only when numbness is persistent, though perhaps fluctuating in its intensity from time to time, that it should suggest that it

was a symptom due to degeneration of the cord. Likewise, when such is the case, there usually occurs a definite tingling sensation and also some slight ataxia and disturbance of bone sensation.

The examination of the blood shows us that the patient has not pernicious anemia. No case of true pernicious anemia ever has as low a color-index as this patient has, while macrocytosis would certainly be evident in a case of pernicious anemia with a hemoglobin of 45 per cent. This patient's red cells average smaller than normal, and not larger. As in pernicious anemia, there is evidence of an increased blood destruction. This is shown by the finding of true microcytes and red cells, with filamentous processes and cells appearing as fragments of other cells. Likewise, there is a definite excess of bile-pigments in the serum and duodenal contents which in the presence of anemia and the absence of definite liver disease clearly suggests an increased rate of liberation of hemoglobin that rapidly becomes transformed to bile-pigment and excreted. The slight enlargement of the liver can be explained as dependent upon this increased rate of the bile-pigment metabolism. One might take the view that the increased output of pigment in the duodenal contents and the increase of pigment in the plasma were due entirely to the inability of the liver to properly maintain the normal pigment metabolism, and that it thus rid itself of pigment that it normally utilized. It may well be that this is partly the cause of the increased pigment output, and that an actual increase of pigment from an increased destruction of red cells is but a partial cause. However, the finding of microcytes and an increased bile-pigment output leads us to consider that this case is one of those in which blood destruction plays an important physiologic part in producing the anemia. The light saffron color of the patient is referable to the entrance of bile-pigments into the tissues from the plasma. It is, however, to be noted that a considerable degree of jaundice of the plasma may occur before the pigments leave the blood for the tissues.

In spite of the blood destruction it is evident that our patient's marrow is being stimulated to produce blood at an increased

rate. This is particularly evidenced by the finding of many immature red cells. Reticulation, polychromatophilia, and fine stippling are signs of youth of these cells. The reticulated cells are 16 per cent. in contrast to the normal number of about 0.7 per cent., while polychromatophilic cells, not present in normal blood, are plentiful, and rarely fine stippling occurs. The occurrence in the vitally stained preparations of a considerable number of cells giving a distinct grayish tint suggests the presence of cells more youthful than normal, but not youthful enough to show reticulation. The presence of a few blasts, cells much more immature than reticulated cells, indicates that the marrow is working under a moderate strain, while the presence of a few early forms of bone-marrow white cells, myelocytes, has the same significance. The marrow is producing the white cell elements satisfactorily, as is especially shown by the number of polynuclears, while the platelets occur in about the normal numbers, indicating a fair production of these elements from the megakaryocytes of the marrow. However, the platelets are not being produced to the degree that the red cells are; for if such were the case, they would occur in distinctly greater numbers.

We are thus dealing with a case that is not pernicious anemia, yet in which there is an increased blood destruction. There is also an increased blood formation, but owing to the predominance of the blood destruction, anemia has become quite marked. Cases of this type may be termed "hemolytic anemia." In the purer forms it is characteristic to find an increased fragility of the red cells to various strengths of salt solution. This patient shows this abnormality, though it is not marked. In any form of hemolytic anemia there is often enlargement of the spleen, associated in some manner with the increased hemolysis, the spleen being larger in the more chronic types. Thus the slight enlargement of our patient's spleen, like the enlargement of her liver, can be associated with the blood destruction. Though enlargement of the spleen usually occurs, but by no means always, when there is increased red cell destruction, marked enlargement of this organ in anemia does not necessarily indicate

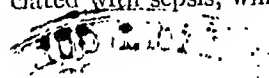
an increased destruction of red cells. For example, the large spleen of Banti's disease is associated with little blood destruction, and the large spleen of myelogenous leukemia is particularly due to an increased formation of white cells.

There are numerous varieties of hemolytic anemia. Our patient in no way resembles acute hemolytic anemia which may result from certain poisons, sepsis, etc. It may be pointed out, however, that acute hemolytic anemia due to sepsis of the endometrium may occur in relation to pregnancy. When such is the case we have the signs of sepsis combined with a very rapidly developing anemia, so that the red count and hemoglobin may fall to 50 per cent. of their original figures in a week's time.

The acquired, congenital, and familial forms of the disease known as chronic hemolytic jaundice are the particular conditions in which the purest type of a chronic hemolytic anemia occurs. The exact cause of these conditions is unknown. The condition our patient has certainly does not belong to the typical congenital or familial forms of this disease, as her history clearly indicates that she had no such disease previous to eight months ago. Her condition does, however, resemble somewhat closely the acquired form of this condition and may be looked upon as one of its subvarieties. The acquired form of chronic hemolytic jaundice presents many various and ill-defined pictures of chronic hemolytic anemia. Typically a patient with acquired hemolytic jaundice presents a history of a very gradual onset of anemia with acholuric jaundice, fluctuating in intensity for some years. The spleen fills the left upper quadrant and the blood changes are similar to those our patient presents. The disease is distinctly favorably influenced by splenectomy, but other forms of treatment are essentially of no value. Such cases may give a history of some previous infection, as malaria and sometimes syphilis, while some cases occur associated with some septic process. The condition that our patient has is best interpreted as one of chronic hemolytic anemia, but when the condition is associated with pregnancy it has, I believe, a much more favorable prognosis than when it is of the chronic idiopathic type.

This variety of hemolytic anemia frequently has been called the pernicious anemia of pregnancy.

True pernicious anemia itself may, of course, start during or following pregnancy, but this condition called pernicious anemia of pregnancy is quite distinct from true pernicious anemia. The literature on the so-called pernicious anemia of pregnancy is rather confused probably because other forms of anemia are associated with pregnancy and may complicate the picture. One of Sir William Osler's last papers was entitled "The Anemias of Pregnancy," and he pointed out that these anemias deserve more study than has generally been given them. It is, of course, exceedingly common to find a slight grade of anemia with pregnancy which is in nowise serious. This anemia may be of a hemolytic nature, and is perhaps a mild form of the severer condition, pernicious anemia of pregnancy. It seems to me that one can find all degrees of gradation from the mild, simple anemia to the severer form. Anemia due to hemorrhage is another type that is associated with pregnancy, while a hemolytic anemia of the acute type dependent upon sepsis may be associated with pregnancy, as has been referred to. There also occurs associated with pregnancy anemia of a more chronic type dependent upon sepsis which may occur during pregnancy or following it. Such an anemia may take a form that suggests a chronic hemolytic anemia, and run a course that may perhaps be indistinguishable from that referred to as pernicious anemia of pregnancy. However, cases of so-called pernicious anemia of pregnancy, a hemolytic anemia developing in a pregnant woman, in the absence of sepsis or other recognized cause, appear to be dependent upon the pregnancy itself, presumably dependent upon a toxemia like eclampsia, and associated in some way with toxins produced in the placenta. Like eclampsia, these cases develop during the second half of pregnancy, and it is said they may develop following delivery. Also, like eclampsia, termination of the pregnancy, provided this is done soon enough, appears to stop any definite progress of the condition. The cases following delivery are commonly associated with sepsis, which in many instances is the only etiologic



factor. In contrast to true pernicious anemia, cases of chronic hemolytic anemia of pregnancy from whatever cause are progressive without remissions, and if cured, relapses occur exceedingly rarely. Like other forms of chronic hemolytic anemia, in rare instances the blood-picture will resemble that of true pernicious anemia. However, the blood-picture is usually of the type seen in the patient before you, and there should rarely be any reason to confuse true pernicious anemia with the rare condition, pernicious anemia of pregnancy, or a chronic anemia occurring in pregnancy dependent upon sepsis.

Pernicious anemia of pregnancy usually comes on gradually over a period of months, with an increased intensity over a few weeks, as occurred in this patient. In some instances it may develop more acutely and run a course of a few weeks or a few months. Termination of pregnancy has permitted cure. However cases are reported where termination of the pregnancy has not stopped the progress of the anemia. It is difficult to tell from the literature what the fatality is in this form of anemia because the cases dependent upon sepsis are confused with the cases apparently dependent upon a true toxemia of pregnancy. Grouping all cases of "severe anemia in pregnancy," the mortality from the literature is 60 per cent. However, in my experience with 5 cases of the same type of anemia as presented by this patient, all recovered except one in the course of a few months following delivery. The cases that recovered had essentially the same degree of anemia as the patient before you. The one that died had a very much severer degree of anemia, the hemoglobin being 25 per cent. This patient died shortly after delivery, and though blood transfusion was advised, it was not done. It is quite possible that in some cases sepsis combined with a toxin resulting from pregnancy has a severer action on the blood-forming and destroying organs than either alone. In such cases the prognosis is probably not so favorable as in the cases where sepsis is not present.

In view of the fact that cases of pernicious anemia of pregnancy are progressive and that the cause appears to be due to the pregnancy, it seems distinctly wise to empty the uterus as



soon as the anemia becomes at all severe. One should not wait to empty the uterus until the condition has reached a point where the patient is seriously sick or the hemoglobin below about 50 per cent., for then a cure perhaps cannot be effected. *If the condition is mild when the diagnosis is established or the hemoglobin above 50 per cent., one may wait some days or even some weeks before terminating the pregnancy provided the patient's general condition together with that of her blood does not become worse.* In this patient, who is eight months pregnant, delivery has been advised in view of the distinct progression of her symptoms in the past few weeks, together with the character of her blood at the present time.

Notes Given on the Case at a Subsequent Clinic.—This patient was delivered of healthy girl twins five days after the above observations were made. It is interesting to speculate whether the anemia was dependent in any way on the fact that there were two fetæ; however, such is probably not the case. The loss of the 3 ounces of blood five weeks before the patient was shown to you was accounted for by a large infarct of one of the placentæ, apparently situated near, but not over, the os.

The patient today, nine days after delivery, appears fully as well as before delivery. Her hemoglobin and red count are essentially the same, but there are fewer reticulated cells (now 8 per cent.), and, most interesting, the fragility of the red cells has become essentially normal. The cells begin to hemolyze in 0.44 per cent. salt solution, while they are completely hemolyzed in 0.28 per cent. salt solution. The fragility does not depend on the number of young red cells. I have observed this same rapid change in the fragility with diminished marrow activity following delivery in other cases. It further suggests that the condition is directly dependent upon the pregnancy *per se*. This rapid change in fragility and decrease of reticulated cells also may occur following splenectomy in typical chronic acquired hemolytic jaundice. The cause of these rapid changes in both conditions may be similar. In the latter condition splenectomy removes at least a part of the cause of the increased blood destruction, and thus allows the marrow to diminish its

heightened activity; while in the former case we conceive the cause of blood destruction is removed by delivery, and thus a more normal balance of blood formation and blood destruction can be established.

There appears to be no reason why our patient's blood should not gradually return to normal. She will probably have a distinctly higher level of her hemoglobin and red cells in six weeks, but it will take some months before the blood can be expected to show a truly normal condition.

CASE II

I have shown you one instance of a moderately severe and rare form of anemia that is curable; one that is exceedingly unlikely to recur. This second patient also has an anemia that is curable provided one treats the disease upon which it depends. The patient is a man, a clerk by occupation, fifty-five years of age, who gives the following history.

Family History.—His father and mother both died of "heart disease" in the seventh decade of life. His brothers, wife, and four children are living and well.

Past History.—Throughout his life he has been a very industrious individual, rarely taking any exercise, and constantly wrapped up in his personal interests. He has had no real vacation in the past twenty years. He neither smokes nor drinks. The only disease he recalls having had is tonsillitis, twenty years ago. For many years he has been constipated, having often gone for several days without a movement of the bowels. However, he has had no abdominal pain, no feeling of fulness, gas, and no nausea or vomiting.

Present Illness.—In the past five years he has gradually gained 50 pounds in weight, so that he now weighs 185 pounds. What bothers him most is that he finds that he tires much more easily than formerly, and feels exhausted at the end of the day. He constantly feels "dopey" and his constipation has become worse, so that during the past year he has been bothered with a definite sense of fulness in the abdomen. He finds that he has become distinctly forgetful and cannot fix his attention. These

symptoms have increased very gradually over the past two or three years.

In the past year and a half, his wife informs us, he has become gradually paler, and for at least six months he has appeared sallow in color. During the past year puffiness of his face has developed. He also notes that he feels better in warm weather than in cold; and he finds he suffers from the cold much more than some years ago. Cramps in the calves of his legs have constantly recurred in the past four years, but have been particularly prominent in the past year. You will notice his voice is husky, that he speaks slowly, and that his speech is thick. He says the change in his voice and speech has gradually developed and increased in the past five years, but that it has bothered him only in the past six months. For about a year he has frequently experienced dull frontal headache. There has been some slight dyspnea on exertion and slight puffiness of his ankles. He has had no other symptoms than those referred to, and it is noteworthy that there is no history of any period of definite improvement in his condition followed by any relapses. It is also to be noted that there is no history of a sore tongue or paresthesia of the hands or feet.

Physical Examination.—You will notice that his mental processes are slow and indecision is rather marked. He appears distinctly overweight, pale and sallow, though the scleræ are not yellow. The skin of his face appears puffy, especially below both eyes, but the skin does not pit on pressure. The skin as a whole is dry, and he tells us he rarely perspires. He says he has lost about half the hair on his head in the past three years, while the hair in the axillary and genital regions is sparse. The hair is dry, but not abnormally coarse. The tongue appears large and thick, pale and rather flabby, but it is not smooth or shiny. The teeth are in good repair. The tonsils and throat are negative. The thyroid gland feels of normal size. The lungs are negative. The heart appears slightly enlarged by percussion. The apex impulse is neither seen nor felt. The heart sounds are regular, but distant, and the first sound is of poor quality. No murmurs are heard. The pulse-rate is 60.

The walls of the peripheral arteries feel definitely thickened, though not markedly so. The systolic pressure is 130; the diastolic 95. The abdomen is large and pendulous. No organs or masses are felt. The genitals are negative. There is a slight puffiness of the ankles, but the skin does not pit upon pressure. The knee-jerks are present, but difficult to obtain. The muscles are flabby and weak. Temperature 97.8° F.

Laboratory Examinations.—*The Blood.*—Hemoglobin, 58 per cent. Red cells, 3,200,000 per cu. mm. Color-index, 0.9 per cent.

The red cells show a definite abnormal variation in size, though they average normal size. Cells slightly larger than normal occur; these are usually round, sometimes a trifle oval in shape, but large macrocytes are not seen. Microcytes are absent. Variation in shape is slight. The red cells stain fairly well, but they appear to be slightly achromic. Polychromatophilia rarely occurs, and the reticulated cells occur in normal numbers. No blasts or other red-cell abnormalities are noted.

The fragility of the red cells is not definitely abnormal.

The plasma contains no excess of bile-pigments.

The white cells are 4000 per cu. mm.

The differential count of 200 white cells is as follows:

Polynuclear neutrophils.....	54 per cent.
Lymphocytes.....	36 "
Large mononuclears.....	10 "
	<hr/>
	100 "

No polynuclear eosinophils or basophils were seen.

The platelets occur in slightly diminished numbers. Their character is essentially normal, though at times a few abnormally large ones are to be seen.

The Wassermann reaction is negative.

The Urine.—The twenty-four-hour amount of urine is 1000 c.c. The specific gravity is 1.012. A very slight trace of albumin is present. There is no sugar. The sediment shows a rare hyaline cast and a few epithelial cells.

The *phenolsulphonethylthalein* test shows an excretion of 40 per cent. of the dye in two hours.

The *stool* is hard and dry, but otherwise negative.

Discussion of the Case.—One might be led to believe that many of this patient's symptoms were due to anemia, and that on account of his history and appearance he had true pernicious anemia of a slowly progressive type. However, he has had none of those symptoms especially characteristic of pernicious anemia. His gain in weight is against such a diagnosis. The blood-picture is not in the least characteristic of pernicious anemia, though an occasional case may perhaps present such a picture at certain times in the course of the disease. Unlike pernicious anemia there is no general macrocytosis, no megalocytes, no microcytes, and there is but slight variation in shape of the red cells. The plasma shows no excess of bile-pigments, which is nearly always present in a case of pernicious anemia, at least when the hemoglobin is below 60 per cent. The low white count with rather few polynuclears and slightly decreased numbers of platelets suggests, of course, a decreased formation of these elements from the marrow. Leukopenia and decreased platelets are a common finding in pernicious anemia, but they do not, of course, indicate this disease. They indicate a decreased output of these elements from one cause or another. In this patient we have no evidence of increased blood destruction, which is a feature of pernicious anemia. There are no microcytes or other cells suggesting that abnormal fragmentation is occurring, and there is no increase of pigments in the plasma. In view of the lack of evidence of blood destruction, it would appear as if this patient's anemia was particularly dependent upon an inadequate or sluggish blood formation. Evidence of decreased blood formation is seen in the leukopenia and decreased numbers of platelets, and there is no evidence that the red cells are being formed at an increased rate.

It might be thought by some that the diagnosis of arteriosclerosis, chronic nephritis, and myocarditis, in a measure dependent upon the type of life he has led, would perhaps be the correct one, and that the anemia was secondary to cardiovascular disease. The character of the heart sounds, slight dyspnea on exertion, thickened arteries, puffiness of his face and

ankles, cramps in his legs, low gravity of the urine, slightly decreased, phthalein excretion, etc., suggest such a diagnosis. The retarding of his mental processes might be explained by cerebral arteriosclerosis. However, cardiovascular disease is not the correct primary diagnosis. You should recognize that this patient presents symptoms that are characteristic of myxedema, a disease dependent upon a disorder of the thyroid function, and materially benefited by extracts of the thyroid gland. There is, however, undoubtedly present some weakening of the myocardium, arteriosclerosis, and probably a slight degree of chronic nephritis. It is comparatively frequent that we find in cases of myxedema arteriosclerosis beyond the degree to be expected from the patient's age, together with a scant amount of urine of low gravity, associated with some impairment of the kidney function. Likewise in myxedema a myocarditis is frequently found, evidence of which is shown by symptoms of incompetency of the heart, together with its slight enlargement and sounds that are weak in character. The blood-pressure is usually low.

This patient's mental torpor and slow, muffled speech, the latter partly attributable to the thickened tongue, are very characteristic of myxedema. The puffiness of the face and ankles you will notice is not a pitting edema due to fluid in the tissues as seen in cardiac and nephritic conditions. It is due to a thickening of the skin and subcutaneous tissues which is characteristic of the disease. The gain in weight, dependent upon an increased deposit of fat and overgrowth of subcutaneous connective tissue, with the large pendulous abdomen, is also characteristic of the disease. The loss of hair, its dryness, his suffering from cold, the subnormal temperature, the absence of perspiration, his sluggish intestinal peristalsis, and his slow pulse, are all symptoms usually found in myxedema. The sallow color this patient presents is one commonly seen in this disorder of the thyroid gland, and it is often more marked. The cause of the color is not clear. In this case it is apparently not dependent upon an increase of bile-pigment in the plasma, though it is possible that such may occur in other cases. Many cases of myxedema show more increased thickening of the sub-

cutaneous tissue than this patient does, especially of the hands and face and in the region of the supraclavicular fossæ.

The symptoms of myxedema are those of a retardation or depression of the various functions of the body. They are probably due to and can largely be explained by a slowing of the general rate of combustion within the body. Thus, the basal metabolism is found distinctly below normal. By determining this we have a further means of establishing or verifying the diagnosis of this disease. Its determination from time to time is also of value in indicating the amount of thyroid extract that the patient should take. The basal metabolic rate in this man has been found to be minus 30 per cent.

It has been pointed out that the anemia in this case was apparently dependent upon a decreased formation of blood. This decreased activity of the marrow is entirely consistent with the diminished activity of the other functions of the body. Thus anemia in myxedema is common in about half of the typical and clear-cut cases. The red count is often reduced to 3,000,000, and sometimes to even below 2,000,000. The hemoglobin is usually reduced in about the same proportion, though more usually slightly greater than the red count, so that a color-index of less than 1 is the rule. However, rarely one may find a case with a distinct increased color-index such as is characteristic of pernicious anemia. Usually the red cells are of the type that occur in simple anemia. Thus they show slight achromia and a variation in size, though averaging about normal size. Microcytes are absent and variation in shape of the red cells is slight. A few polychromatophilic cells may be found. Greater changes in the red cells are seen with the lower counts, and even blasts may appear. The white count is often low, and the differential count may show a slight lymphocytosis. The platelets are often decreased. It has been pointed out before that a decrease of bone-marrow white cells and platelets may be taken as indicative of decreased activity of the marrow. Fluctuations in the white count and platelets occur in this disease, dependent upon the state of the marrow, so that it is not uncommon to find at times a slight increase of the bone-marrow white cells as well as the

platelets. In the rare case with a distinct increased color-index, a general macrocytosis occurs and a few microcytes may be found, so that the red cells may resemble those seen in typical pernicious anemia. No observations have been made in such cases on the bile-pigment metabolism to indicate whether there is any definite abnormal blood destruction or not. On account of the occasional case that shows a macrocytosis with the presence of microcytes and a decrease of white cells and platelets, the whole histologic blood-picture in myxedema rarely may be indistinguishable from that of typical pernicious anemia.

Some severe cases of myxedema have recurring nosebleeds, and at times hemorrhage from other mucous membranes. They may also show purpura. It would appear that the bleeding in some of these cases is associated with a definite decrease of the platelets. A somewhat prolonged coagulation time of the blood may be found, and this may contribute to the hemorrhages.

Myxedema is not difficult to recognize when the symptoms are at all marked. The condition is much more common in women than in men. The milder cases are not uncommon, and are often overlooked because one is apt to forget the condition unless the clinical picture is borne in mind. The rare case, giving a blood-picture resembling that of pernicious anemia, like other cases of myxedema may appear sallow as well as pale. Thus such cases may closely simulate by their appearance as well as by their history and blood true pernicious anemia. The finding of a distinctly low basal metabolism will distinctly favor the diagnosis of myxedema. This finding taken together with careful attention to the patient's appearance and symptomatology will enable one to distinguish these two conditions that may rarely simulate each other rather closely.

The treatment of myxedema is to give some active preparation of the thyroid gland. The amount to be given will vary in each case; 1 to 2 grains of thyroid extract three times a day is usually a suitable amount to begin with. The subsequent amount will vary according to the results produced. The patient must, however, continue through life to take at least a small amount of an active thyroid preparation. One symptom

to guard against during treatment is the occurrence of precordial pain, often associated with a rapid pulse. If this develops, the dose of the thyroid extract should be cut down and the patient advised to remain in bed. The effect of suitable treatment is quickly evident by the improvement in both the physical and mental symptoms. We may expect this patient before you to have his memory and speech return to normal, and, in fact, return practically to normal in all respects. There will be improvement in the abnormal signs referable to the cardiovascular system, and he need not be alarmed about the state of these organs. His anemia will improve coincident with improvement of the functions of the body. In addition to his thyroid medication, it would be wise to curtail slightly the amount of carbohydrate and fat that he eats so as to aid in the reduction of weight, which will particularly occur as the result of thyroid medication. This patient also should be directed to take suitable exercises to increase the tone of his muscles. Proper directions should be given to alleviate his constipation, which may be dependent partly upon his disease.

Though these two cases I have shown you bear but a superficial resemblance to each other in that they both have a distinct anemia, I wish to call your attention to the fact that such cases are mistaken for pernicious anemia as well as for other conditions. The cause of the anemia in such cases may not be recognized. It is most important to recognize the cause, for in both instances proper treatment when undertaken early enough will cure the patient. In the first case the cause is pregnancy, and the chief treatment is to empty the uterus. In the second the cause is myxedema, and the treatment is thyroid medication.

CLINIC OF DR. FRANCIS M. RACKEMANN

MASSACHUSETTS GENERAL HOSPITAL

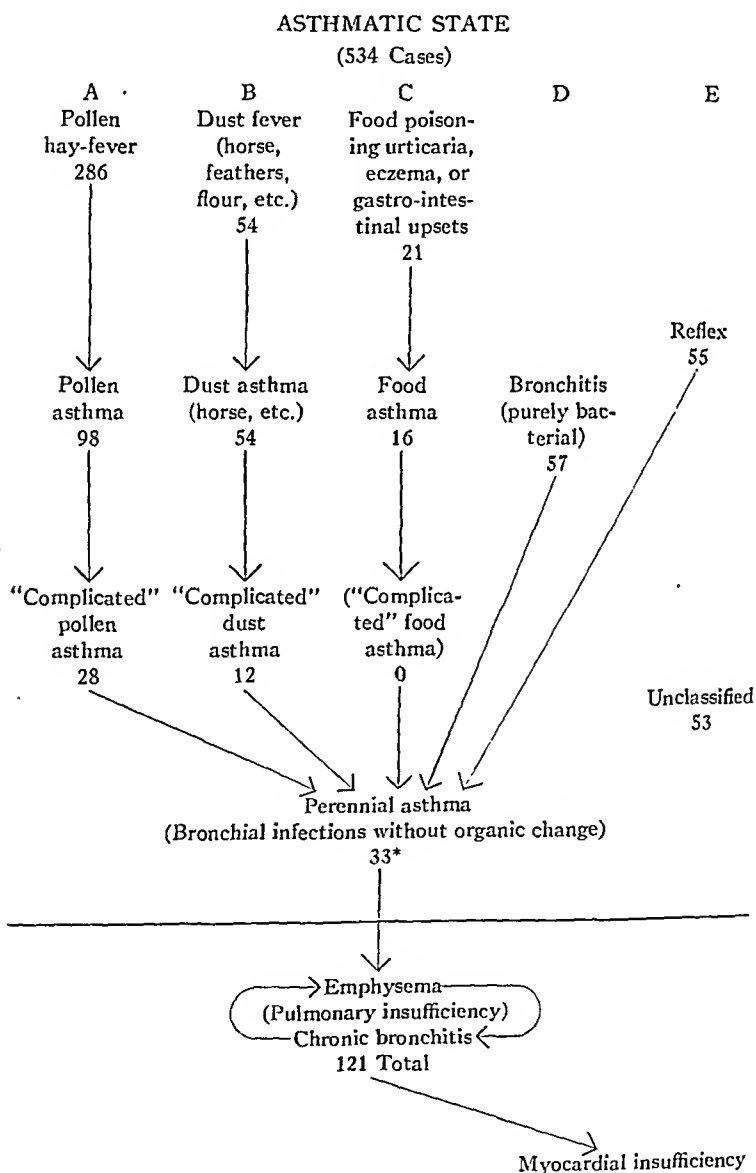
THE VACCINE TREATMENT OF ASTHMA¹

THE treatment of those cases of asthma which fail to give a skin test to the ordinary foreign proteins which exist as food or as some animal dust is always difficult. Such cases demand the closest study if the ultimate result is to be successful.

I should like to discuss with you this morning several cases representative of this group of asthmatics. If you will look at the accompanying chart on page 1752 you will see exactly where these cases of bacterial asthma fit.

This chart is an attempt not only to classify cases of asthma, but to show the relationship which exists between the various types. The arrows on the chart show clearly the gradual development which takes place in many cases from a less severe to a more severe and more advanced stage of asthma. For example, an old man of fifty years comes in for "asthma." As a boy he had hay-fever, at about eighteen years of age he had his first attack of asthma with his hay-fever, and thereafter until the age of about twenty-eight this pollen asthma occurred every September and lasted until the first hard frost. At the age of twenty-eight the pollen asthma for the first time lasted longer than the first frost and, in other words, was "complicated" by some bacterial infection. At the age of about thirty-five this asthma occurred not only during September, October, and November but also appeared for the first time in February and again in April (perennial asthma). Finally, about six years ago he had asthma practically all the time, and between the severe attacks, instead of being comparatively well, he had more or less

¹ From the Anaphylactic Clinic of the Massachusetts General Hospital, Boston.



* New cases originating in this group.

constant shortness of breath on exertion and some chronic cough, so that the emphysema which he now has is undoubtedly of about six years' duration. Such a history is not uncommon, and the ability to trace the various stages is usually possible if the patient is reasonably intelligent.

Such a development and change in the progress of the asthma can be traced in the history of many cases, which shows the importance of careful study, and such careful study is well worth while. For example, two years ago a gardener working on a private estate was seen in October with very severe asthma, which he said began each year early in September and lasted until the cold weather. He gave a beautiful test to ragweed, and treatment with ragweed extract the succeeding summer was so successful that during that fall he had asthma only on three nights, and during that winter was very much better than he had been for a long time. When seen he, of course, had a bacterial asthma based upon a foreign protein background. Treatment of the background was, therefore, the keynote to the treatment of the bacterial complication.

The chart demonstrates other groups. The cases in the upper left half of the chart include all the cases giving a positive skin test. The numbers on the chart show the number of patients originating in the various groups and also the number who have developed from above downward, from simpler to more advanced stages of their disease. For example, there were 286 cases of pure hay-fever. A certain number (34 per cent.) developed pollen asthma, and 28.6 per cent. of these with pollen asthma, or about 10 per cent. of the total hay-fever cases, went on to develop a complicated pollen asthma—that is, developed a bacterial infection on top of the original pollen asthma. Those numbers marked (*) represent the number of new cases developing in that group. This heavy line separating perennial asthma from emphysema represents the "line of organic change." If any patient above the line is examined physically between his asthmatic attacks no defect can be found, but when once chronic emphysema has developed the barrel-shaped, hyperresonant chest, with prolonged, high-pitched breathing remains permanently present.

Patients with bacterial asthma may be still further divided, as I will try to show by the cases later. Primarily, however, there are those who have emphysema and those who do not.

Anatomically, emphysema is a condition in which the alveoli in the periphery of the lung are very greatly distended, so much so that the blood-vessels running in the alveolar walls are often obliterated, so that on account of the impairment in nutrition of these alveolar walls ruptures take place and several alveoli coalesce. This is the probable reason for the hyperresonance, the high-pitched breathing and the barrel chest which is so characteristic of the chronic cases. Cyanosis often accompanies this condition. This cyanosis is not due to the breaking down of the peripheral alveoli, but depends upon the fact that the impaired distention of the lungs prevents the usual and adequate expansion of the central portion. Comparatively little blood can get to the periphery, so that most of the blood must flow through the alveolar capillaries in the central parts of the lung where, because of the inadequate expansion, it is improperly aërated and cyanosis results.

In addition to the improper aëration there is in most of these cases a greater or less infection of the bronchial mucous membrane, which causes edema and low-grade inflammation. This, by obstructing the free flow of air, still further hinders the proper absorption of oxygen by the blood. All of which explains why in the presence of respiratory infection, associated as it is with considerable thick purulent sputum, the cyanosis is more marked than in the same cases at the time when the sputum is much less in quantity and much clearer in character.

This condition of emphysema may be simulated during a severe paroxysm of asthma and disappearing with recovery (the alveoli are greatly distended, but not ruptured); or if the paroxysms are frequent and close together, true emphysema gradually develops into the chronic stage described above. Emphysema may be the only anatomic change associated with asthma. Cases of asthma who have no emphysema when examined between the attacks may be found to be normal in every way.

I will show you first several patients who have no emphysema.

The first case is a man of thirty-four, who since the age of about twenty-two has had severe "colds" pretty regularly in the spring and fall (in April and September), which colds have been pretty regularly followed by attacks of asthma of greater or less severity. During the first few years these attacks lasted only a day or two, but recently and in the past two years they have been much more severe, so that last fall he was confined to bed for three weeks with severe paroxysms of asthma every night for most of that time. This asthma would awaken him at 4 A. M., and from then until morning he would be very uncomfortable, having to get out of bed and burn asthma powder, until finally the attack would pass off about 8 A. M., when he could raise a considerable quantity of thick, tenacious sputum containing a few yellowish streaks. During the past winter he has been perfectly well until he came to the hospital three days ago with a recurrence of his usual spring attack. His physical examination is negative except for his chest, which is hyperresonant and full of all manner of squeaks and musical râles. His lips and finger-nails are cyanotic; the blood-pressure is rather low (115/80). In other words, he has an acute emphysema. Skin tests to all the common proteins are entirely negative, and, as a matter of fact, there is nothing in his history to suggest that proteins are a factor, as the attacks are not preceded by any change in his diet or in his occupation, and, indeed, four years ago, while traveling through the South in the fall, he escaped his usual attack. His sputum is small in amount and consists of thick tenacious mucoid material with a few whitish flakes. There is a good deal of froth on the top of it. When I pour it on to a Petri dish and hold it against a black background I think you can see those rounded glistening masses looking like tapioca—the pearls of Laennec—which are found not uncommonly in sputum of this type. Those small coils of whitish material are Curschmann's spirals. Neither of these formations has any great significance.

Day before yesterday this sputum was smeared on a blood-agar plate, and now there is, as you see, a good growth. There is no really predominant type of colony, but there are plenty of minute pin-point greenish colonies, others have a faint zone

about them—"checker" colonies probably of non-hemolytic streptococci—and finally there are a number of these larger opaque dome-shaped colonies which are pink in transmitted light, some are staphylococci, others diphtheroids. Many other colonies probably could be identified.

This second plate is, as you see, divided by the red pencil into sections, each of which was inoculated yesterday with one of the many colonies from the original plate. You can see what a good growth there is and how easy it is to tell whether this growth is pure or not. Theoretically, such cases as this man represents should be the ones best suited to vaccine treatment, since it ought to be possible to immunize him actively against the offending organisms and thus prevent his further attacks. The difficulty, of course, lies in the fact that it is difficult or impossible to tell what is the causative organism. At present we have no direct information as to whether the bacteriology of cases of this type varies from time to time or not; in other words, as to whether each attack is caused by the same or by a different organism. The treatment of this particular case should be now absolute rest in bed until this present acute attack is over. Adrenalin or atropin, or both, should be given as necessary, and will probably relieve acute paroxysms. Potassium iodid will make his sputum thinner and easier to raise. Bicarbonate of soda in teaspoonful doses in water three times a day is a harmless and often helpful addition. On the theory that the next attack will have the same bacterial cause, the culture from his sputum ought to be kept on hand, so that about six weeks before his next expected attack a course of vaccine treatment can be started.

In March I saw a very similar case who came in to say that his usual spring attack was overdue. He had received vaccines made at the time of his fall attack, and said that he felt so much better that he thought the vaccine treatment would prevent further trouble—and, so far, it has.

Closely related with this first patient is this second man, a powerful, well-built Irishman of forty-five, who one week ago was taken with an extreme attack of asthma requiring of his own doctor large doses of adrenalin, morphin, hyoscin, and atro-

pin to give him even a little relief. He has had this asthma only for a year. It comes on in isolated attacks, each of which has been fairly definitely associated with a cold or with exposure. There is a strong alcoholic history, and the past three attacks have each been directly associated with a drinking bout. Three months ago in the winter he had his usual attack, but the asthma has failed to clear up in the meantime, so that a little chronic cough and a considerable wheeze, especially marked in the early morning hours, has persisted from week to week. The present acute exacerbation probably represents a fresh respiratory infection. Like the first man, his skin tests are entirely negative, and there is no particular reason to suspect a foreign protein cause. His blood-pressure is high (160/90), his arteries are a little hard; the liver edge can be felt; his skin is soft and silky; face, as you see, is ruddy and congested. He has paroxysms of severe racking cough, finally resulting in the raising of a very thick purulent mass of sputum which at times is streaked with blood.

The essential treatment of this man must be constitutional; to so regulate his life and diet that his circulation and kidneys will be improved and his lung volume increased, with rest in bed or in a comfortable chair, until the worst of the present attack is over. Adrenalin is about the best known remedy for his dyspnea. Digitalis may be indicated later. In addition, the man's teeth and sinuses will be eventually investigated for some focus of infection which can be surgically removed, and his bowels ought to be regulated.

The bacteriology of his sputum is very much like that of the first man, except that there is a well-marked predominance of the small greenish pin-point colonies, and a vaccine made of this may help him, and is worth a try.

A case of this kind is very prone to develop permanent and chronic emphysema, a condition which obviously complicates the treatment, and in view of the story of several months' pretty constant symptoms it is probable that he already has such a complication.

The third patient has emphysema. He is an Italian laborer

of fifty-two who has had asthma now for ten or fifteen years which troubles him nearly all the winter, beginning each fall with a severe attack in the month of October. During the summer he is, like almost all patients with emphysema, comparatively free of asthma and can do his work normally. He illustrates a very important point. Skin tests with foreign proteins are *not* all negative. He gives a fairly definite test to ragweed pollen, and it seems that last year his asthma did begin in August and he was very uncomfortable during August and September, so that the question of treating him with ragweed during this coming summer is a very important one, which must be decided correctly. Further history reveals the fact that last year during August and September he had absolutely *no* symptoms in his eyes and nose; furthermore, that the attack began during *the first week of August* (the hay-fever season in Boston began in 1920 about August 17th), so that at the present time it seems best, considering his age and present condition, to ignore this positive test (unless the history is later found to be incorrect), and to regard him as a purely bacterial case, assuming that some respiratory infection, perhaps following exposure, was responsible for the trouble last year. This man has been followed in the clinic during this past winter and has had six doses of a vaccine, which, however, did not help him.

I should like now to say something of the use of vaccines in general and the selection of vaccines for treatment, a matter of considerable importance for the reason that I have several times observed that whereas the treatment with a first vaccine was of little use, that when the organism was changed, the good effect was quite marked. Walker¹ has made similar observations.

In 1920 I stated in a paper on "The Relation of Sputum Bacteria to Asthma"² that vaccines were successful only in case some local reaction in the arm followed the subcutaneous dose. At that time my method of selection was to isolate individual organ-

¹ Walker, I. C.: Treatment of Bronchial Asthma with Vaccines, Archives of Internal Med., 1919, xxiii, 220.

² Rackemann, F. M.: The Relation of Sputum Bacteria to Asthma, Jour. of Immunology, 1920, v, 373.

isms from the patient's sputum; to make vaccines of each and to do a series of intradermal skin tests with these vaccines. The selection of the proper vaccine for treatment was based upon the local reactions produced. Results of treatment were quite satisfactory. In the presence of a positive test 16 patients were treated and 14 did well, while in the face of the negative tests 10 patients were treated without any success at all.

Since then it has been found that certain organisms are irritating, since with them "positive tests" are obtained in the majority of individuals tested, so that while the idea is probably correct, the technic may be misleading. Since that time I have been giving patients small subcutaneous doses of each vaccine obtained, and then planning further treatment according to the local reactions in the arm resulting from these subcutaneous doses.

It is all too common to give vaccines without local reaction and under these conditions it is easy to rapidly increase the dose, but unfortunately such increases cause no local symptoms in the arm, nor do they cause any change in the asthma at the time, and the ultimate result is usually not good. When, on the other hand, local reactions are well marked with pain, tenderness, and some induration, which lasts for twelve to twenty-four hours, and when the asthma is temporarily worse, the ultimate result is usually good. Subsequent doses must be made relatively small and treatment must be given cautiously.

When successful, good results will occur usually before six doses have been given, so that I feel now that it is useless to prolong the treatment further than a series of this size unless some definite reason is apparent.

Coming back to this last patient and the fact that his six doses in the winter did not help his asthma, it may be said that at no time did he have any local reaction at all. The hope now is to locate some organism which grows in reasonable numbers and which at the same time will produce a vaccine to which he will give a definite positive reaction.

I might give you some figures as to the results of sputum examination and vaccine treatment as found during the past year in this clinic. As to sputum examination, there were 33 speci-

mens of the purulent type. Smears showed a variety of organisms without predominance in most cases, but on blood-agar plates a predominant organism occurred in 21 of the 33 specimens, and included:

Green streptococcus	in 8 specimens.
Staphylococcus	in 5 "
Pneumococcus	in 3 "
Non-hemolytic streptococcus	in 2 "
Gram-negative coccus	in 2 "
Hemolytic streptococcus	in 1 specimen.

There were 41 specimens of the thin mucoid type. A predominant organism occurred in 20, which in 17 cases was a streptococcus—hemolytic in 4. Staphylococci were found in only 1 specimen.

Hemolytic streptococci were found in only 21.2 per cent. of the purulent specimens, whereas in the clear specimens they were found in 51.2 per cent.

In several cases the same sputum was studied several times at intervals. Even without vaccine treatment the sputum bacteriology was often found to change. For example, it was noted that when the sputum became thinner and less purulent, staphylococci tended to decrease in incidence, whereas hemolytic streptococci were found in greater numbers. These spontaneous changes should make us cautious about attributing too much to the use of vaccines.

In this work only autogenous vaccines have been used. Only about 50 cases have been treated adequately—a small number considering the many different kinds of cases included. I shall not attempt to give you any details, but will say simply that only about half the cases had asthma without emphysema, and of them only about half were helped by vaccines, while of an equal number of cases with emphysema only a third were helped. Furthermore, treatment with a predominant organism gave no better results than with any other organism selected as described above.

I want to show you 3 other cases which illustrate other methods of treating these non-sensitive patients.

The first is a girl of sixteen years who lives on a farm and who has had asthma in short attacks at fairly frequent intervals through the winter, while in the summer she is fairly well. She was in the hospital last fall, and at that time skin tests were all negative and she was put down as a bacterial case. In the Throat Department a diagnosis of vasomotor rhinitis was based upon the typical boggy, edematous appearance of her nasal mucous membrane, for which there was no definite cause in any of the accessory sinuses nor in the tonsils. A staphylococcus vaccine was made from her nasal secretion—she had almost no sputum—and she was given several doses of this with very slight local reaction, but without material effect upon her asthma. Quite recently, her asthma being rather worse, she was restudied. Skin tests by the scratch method were still negative; by the intradermal method, however, a slight but fairly definite reaction to horse hair extract was obtained. Careful questioning brought out the fact that the house is connected with a stable. The farm was visited. The place was very dirty and dilapidated. The kitchen connected directly through a harness room with a grain room and barn, where four horses and two cows are kept. The cows wander on all sides of the house, as do hens and chickens. The three small brothers have a pony which they play with in the afternoon. A large dose of horse dust occurring daily is easy to understand, so that about six weeks ago treatment was started with horse hair extract, with the result that so far at least she is considerably better and the hope of relieving her asthma is fairly definite. Last summer she spent two weeks at the seashore, where they had no horses, and during this time she had absolutely no asthma.

One point of interest is that when the diagnosis of vasomotor rhinitis was made last fall, further and more careful attention should have been paid to it. Such a condition is not common with pure bacterial asthma, but is very common in most of the cases of asthma due to the inhalation of foreign protein in the form of dust. It is, of course, seen most typically in hay-fever, and, as you know, hay-fever was formerly labeled simply "seasonal vasomotor rhinitis." It is also seen in cases of pure horse asthma,

in bakers who have asthma from inhaling the dust of flour, and in other conditions. The old-fashioned "chronic catarrh" is today represented by this vasomotor rhinitis. If we exclude the cases of hay-fever and the typical cases of horse asthma, in other words, those cases in which the relation to foreign protein is perfectly obvious, it is found that only about 12 per cent. of the remaining cases are due to some foreign protein. In other words, although many cases have been tested with food and dust proteins by the cutaneous method, only about 12 per cent. have been found to be positive. Where asthma depends upon some foreign protein, as in dust, a chronic vasomotor rhinitis is pretty regularly found as an accompanying condition.

This girl illustrates a further point of interest in that negative skin tests may be misleading. Last fall all tests by the cutaneous method, including the test to horse hair, were entirely negative, and it was only when the peculiar circumstances of her life were investigated and the cutaneous method checked by the intradermal method that the positive test to horse hair and, consequently, the key to the whole situation was discovered. In other words, as I have tried hard to emphasize throughout this work, a careful and accurate history with an exact knowledge of the circumstances of asthma is, after all, of even greater importance than any findings by skin tests. This is, of course, undoubtedly due to the fact that our methods are still relatively crude.

The second patient is a large, obese Italian woman of thirty-eight, whom I first saw last fall when she came into my office wheezing dreadfully, weeping and wailing at the same time in a very excited upset state. She said that she had been in a similar condition throughout the summer and that the doctor had visited her at least twice every day for three months, to give her large doses of adrenalin. It was quite obvious that hysteria was at least a very important factor in her present condition regardless of the true underlying basis. Skin tests were all negative. She was definitely cyanotic, with evidence of pulmonary emphysema. She had a dry, hacking cough and raised a small amount of thin, glairy mucus which contained no pus. It was decided to give

her doses of her own defibrinated blood as originally described by Kahn and Emsheimer.¹ It was felt that this would do more than anything else to satisfy her present hysteria; 25 c.c. of blood were drawn from her arm vein and in a sterile test-tube was defibrinated by stirring with a sterile glass rod. At the end of ten minutes a clot had collected around the rod, which was then removed, and the defibrinated blood was poured through sterile gauze into a clean tube and eventually injected subcutaneously into the soft tissue of her thigh. The patient felt better right away. She returned in a week to say that the doctor had seen her only once. After four similar treatments she was practically cured. She returned again in six weeks with another attack, had another treatment, and was well for another six weeks. The intervals between attacks has been throughout this winter longer and longer, but she still must come in every six to ten weeks for further doses of her own blood. Whether this treatment acts in a non-specific manner to stimulate the production of specific antibodies, according to the mechanism described by Hermann,² or whether the rather dramatic procedure carried on in her presence has an entirely mental effect, I do not know. She is of great interest as illustrating some of the methods of dealing with asthmatics and the importance of selecting different cases for different forms of treatment.

Finally, I would tell you of a tall, pale, thin-faced, slender girl of nine whom I first saw last fall, when she said that she had been having asthma at regular weekly intervals each Sunday for several months. The mother was sure that some food was responsible, and on the advice of the doctor milk and eggs had been withdrawn. Physical examination showed a child obviously underweight. The chest was long and thin, with heart apex in the sixth space, the shoulders were very round, so that the neck and head projected anteriorly; the front chest was quite flat and the abdomen was prominent.

¹ Kahn and Emsheimer: Autogenous Defibrinated Blood Treatment of Bronchial Asthma, *Arch. of Internal Med.*, 1916, xviii, 445.

² Herrmann, S. F.: Liberation of Antibodies on Injection of Foreign Proteins, *Jour. Infec. Dis.*, 1918, xxiii, 457.

Skin tests were done, found negative, and later repeated in order to satisfy the mother that the child could take all foods without difficulty. The diet was rearranged and balanced properly. Her school lunch was adjusted so that she had two hearty sandwiches and no cake. Regular play and exercise out of doors was insisted on, and, in addition, arm and chest exercises were prescribed. Hydriodic acid was given temporarily. When seen a month later the child had gained 4 pounds, looked entirely different, and had had no asthma at all for the past two Sundays. (Why she picked out Sunday was never discovered!)

To sum up: I hope I have demonstrated the necessity of careful history taking, physical examination, and general study as a preliminary to the treatment of asthma.

Each new patient with asthma presents a definite problem for solution, and the study should be carried out with this point in view. Practically no two cases are alike, and this fact, of course, really accounts for the difficulty of putting together any satisfactory classification of cases. It also explains the difficulty of satisfactory treatment and perhaps explains why such methods as vaccines do well in some cases and not in others. Of course, certain cases are fairly typical and can readily be grouped together, and these cases I have tried to indicate in the chart. Patients like this last small child and like the excitable Italian woman I have grouped together under the head of reflex asthma, believing that by some unknown mechanism asthma may in certain cases be simply reflex in character. The few patients in whom foci of infection in tonsils and teeth can be identified and subsequently proved by appropriate surgical treatment to be a cause of asthma, should also belong in this reflex group. This, of course, is still another method of treating non-sensitive patients. It might be possible to speculate a little and offer the thought that in such cases there were two underlying factors. First, the focus of infection itself, and secondarily a tendency to asthma, by which I mean that these patients for some unknown reason have as a result of the focus an attack of asthma rather than have chronic arthritis or periodic headaches, or any other of a relatively large group of chronic maladies which are today

recognized as being in many cases due to the presence of such a focus of disease.

From such a point of view we may be able to study these cases with greater advantage. When there is a positive family history of protein sensitiveness this tendency to asthma becomes more easily explained.

Where in many asthmatics there is a chronic infection of the bronchial mucous membrane, this may, of course, act directly to cause or to assist the bronchial spasm. On the other hand, it may act in a reflex manner, much after the infections in teeth and tonsils. Bronchial infections cannot be removed surgically, but, on the other hand, can sometimes be treated by producing an active immunity with the corresponding organism, and this represents the rational of vaccine treatment in asthma.

As I have tried to emphasize, vaccines seem to work better in some cases than in others, and, furthermore, vaccines of one kind may give relief to a patient where vaccines of another kind do not. I hope I have made it clear that in many cases vaccines are not necessary at all, and by obscuring other and much simpler measures of treatment may do harm.

Finally, I would again emphasize that vaccines produce only an active immunity. They should be used with great care in the presence of an acute infection. It is well known that "a negative phase" follows their injection, and I have seen well-marked and at times quite prolonged exacerbation of asthma following their use. Their greatest use is in the recurrent type of asthma, where, by producing a degree of active immunity, the hope of preventing or modifying the next attack is not unreasonable.

CLINIC OF DR. JAMES P. O'HARE

PETER BENT BRIGHAM HOSPITAL

A CASE OF VASCULAR HYPERTENSION WITH ANGINA PECTORIS AND CEREBRAL HEMORRHAGE. AUTOPSY¹

In this clinic I am presenting to you a case of hypertension which is rather extraordinary in that it illustrates so many phases of vascular disease. The case has been followed for six to seven years and, what is extremely rare in these patients who die suddenly almost anywhere except in the hospital, it came to autopsy.

The patient, a married woman of fifty-one, entered the Peter Bent Brigham Hospital first on November 10, 1914. Her blood Wassermann had been found positive in the Outdoor Department a few days before and she was sent into the hospital for lumbar puncture. Her family history disclosed only one important element—her father had died of heart trouble. Her marital life had been rather stormy. She had been married twice and had separated from her second husband about five years previously. As a result she was supporting herself and working very hard. She had had one daughter and no miscarriages.

Her past history was as follows: Measles and pertussis in childhood; typhoid at twenty-three; numerous attacks of tonsillitis, pharyngitis, and laryngitis. An ovarian cyst was removed at thirty-four, and she had a total hysterectomy with artificial menopause at thirty-five. This change of life was apparently without symptoms and uneventful. In 1914 a laparotomy was done for removal of numerous adhesions. Occasionally and for

¹ From the Medical Clinic of the Peter Bent Brigham Hospital.

an indefinitely long time the patient had a dull frontal headache. Occasionally, too, there had been some ringing in the ears. At times, when very tired, there was palpitation, and when exhausted or after a severe effort or when walking in the face of a strong wind she noted a sharp stabbing pain over the heart radiating up into neck and into the back. There had been no evidence of cardiac decompensation in the form of edema of feet or ankles. For years she had had a chronic cough with occasional blood-tinged sputum. The blood, she said, was "from her throat or nose."

Her habits had been good; tea, one cup a day; coffee, two a day; no alcohol. She had always worked hard physically, and had much cause for worry, although she did not seem to be of a nervous or worrisome type.

Her present illness began about three years ago, when she noticed that she was beginning to tire easily and that she had marked weakness of the limbs. There was a dull ache over her eyes and, off and on, ringing in the ears. Since her last operation there had been occasional pain in the right lower quadrant and tenesmus. Because of the double plus blood Wassermann she was sent into the hospital for lumbar puncture. Physical examination at that time showed the following important points: The heart's apex impulse could not be felt and, furthermore, the left border of dulness could not be determined because of gastric tympany. The first sound at the apex was of marked intensity and was followed by a loud blowing systolic murmur, which diminished in intensity toward the base. It is important to note that there was no rough basal systolic murmur at this time. The pulmonic second sound was slightly accentuated and greater than the second sound in the aortic area. The heart rate was essentially normal. Radial vessel walls could not be palpated. The blood-pressure was 210 systolic and 120 diastolic. Reflexes were all equal and active. Lumbar puncture was negative. (It may be said that throughout her illness it continued to show no abnormalities.) A single specimen of urine showed negative findings except for a low specific gravity (1009). Phthalein excretion in two hours and ten minutes was 48 per

cent. Blood counts and smear were normal. The patient was discharged the day after entrance, having entered merely for a lumbar puncture.

Let us analyze in detail some of the important and interesting aspects of this patient at her first entry. The first thing worthy of comment is her age—fifty-one. This case was evidently a case of vascular hypertension, although at this entry and subsequently she was diagnosed, by mistake, chronic nephritis with hypertension. Female patients with this disease usually appear at the clinic or in the office during or just after the menopause, and there is pretty good ground for thinking that the changes taking place in the endocrine glands at this time play a part in this condition. Fifty-one, then, is not an unusual age for such a patient to discover that she has high blood-pressure. But right here we note an extraordinary condition in this woman. A hysterectomy with a consequent artificial menopause was performed at the age of thirty-five. Could the increased tension have developed at that time? We know that high-pressure patients not very infrequently live fifteen or more years. It seems to me, however, that in this particular case it is more likely that the vascular disease originated about a decade later, at the more usual time. The patient, you may remember, had an uneventful menopause. Perhaps we might assume that the relation between chronic vascular hypertension and the menopause demands that all or at least several of the endocrine glands be effected. When a complete hysterectomy is done these glands are perhaps not so uniformly effected as during the normal menopause. The next important factor to consider is the family history. In this we note that the patient's father died of heart trouble. Of course, it must be remembered that any patient with any disease may have a progenitor who died of heart trouble. Nevertheless it is a significant fact that a large proportion of cases of vascular hypertension have a family history of heart or kidney disease or apoplexy. In 153 cases at this hospital, 68 showed such a family history of circulatory disturbance. Furthermore, if we delve searchingly into the early history of our patients we not infrequently find other

evidence that they have probably been born with a subnormal circulatory apparatus. Not infrequently these patients tell of profuse hemorrhages from the nose coming on with little or no cause in early life. These nosebleeds were much more frequent than in their associates. The usual story is that they began near puberty and continued well into adult life. For some reason they have ceased in most cases at or about twenty-five years of age, and have then reappeared again from thirty-five to forty-five. Vasomotor disturbances, too, seem to be more common in the early history of such patients. It is hard to avoid the deduction that one's ancestry may be, in part at least, responsible for his circulatory woes. It seems also to indicate that those who have such a family history should be cautioned to avoid those strains and stresses which seem to play a part in the production of premature arteriosclerosis, hypertension, and old age.

Let us now consider this woman's past history. The history of measles, pertussis, typhoid fever, and many sore throats does not present us any very definite infectious etiology on which to lean. As a matter of fact, it has been our feeling that infections probably played but little direct rôle in the production of vascular hypertension. At least we can say that in our cases infections do not seem to be any more common—or more specific—than in any other group of cases. Even syphilis, which is known to produce arterial disease, does not seem to be more prevalent in this condition than in the average run of hospital patients. Our records show that 12 per cent. of our medical cases have syphilis. They also show that 11 per cent. of our cases of hypertension have syphilis. In the case we are discussing a positive Wassermann was repeatedly found, and perhaps it did play a part in the disease.

The patient had been twice married and apparently not happily. The latter has necessitated self-support by much hard work and the patient has had much cause for worry. This is of the greatest importance. Of all the possible causes of vascular hypertension only two stand out, and these in surprising constancy—a family history of vascular disease and hard, worrisome work. The business man who has been struggling for years to

establish his business by working day and night and refraining from taking those more than necessary vacations is fairly typical. In such do we find early the symptoms which eventually compel him to slow down. This fact cannot be overemphasized. It is the nervous, worrisome, constant, high-tension work that produces premature old age, arteriosclerosis, and its various effects. Only recently I have seen an extraordinary example of this and of the selective action of the vascular disease at the point of greatest stress. A banker of fifty-nine who had a well-marked family history of arteriosclerosis came to Boston to see if we could find any remediable cause for the arteriosclerosis which had resulted in his blindness. One year before he had lost the sight of his right eye from a thrombosis of the central artery. Recently the other eye had suffered a similar fate. His life had been an exemplary one and he prided himself on the fact that he had worked harder than any one else in his institution. Every morning he went to the post office and gathered the bank's mail and had read and digested it before the bank was open. During the day he was in constant demand. So filled up was his time that at lunch he "merely went across the street" and gulped down one of those tabloid meals—a "coffee-egg-malted milk" or something similar. His existence seemed to be confined within a circle bounded by his home and his office. No machine could stand such a life indefinitely. After twenty-five years of such activity the most overworked part began to wear out, the cerebral vessels, especially the retinal. It is of interest to note that in this man there was no evident arteriosclerosis anywhere except in his brain. It is also of interest that there was nothing in the way of an etiologic factor but his constant, unrelenting hard work. The conclusion follows that it pays to play. Unfortunately, in the poor woman we are considering she had no choice. She had to work hard and necessarily worried to "make both ends meet."

One of the symptoms this patient presented in her first entry is worthy of comment. You may remember that she had had a dull frontal headache for some time. In hypertension, while a frontal headache is not uncommon, the sub-

occipital headache is more frequent. It has, curiously enough, several peculiar characteristics. Usually it is an early morning headache which the patient has on awakening. It seems to be due to congestion within the cranial cavity. Merely changing from the reclining position to the upright does not dispel this distressing symptom, but activity of any sort usually causes it to disappear. The mere whipping up of the circulation, by means of a cup of coffee, without any other change will frequently cause it to disappear. Another curious fact about these headaches in high blood-pressure is that the headache does not run at all parallel to the height of the tension. One individual may have an excruciating headache with a pressure of 200 systolic and 110 diastolic, whereas another may have none with 260/140. Furthermore, in the same individual it seems as if a compensatory process takes place. For a year or more he may have fiendish headaches with a pressure averaging 200 systolic and 110 diastolic. Later, however, when his pressure has risen to 260/140, the headaches may be entirely absent.

In the physical examination and laboratory findings there are but two elements on which I wish to comment at present. One is the condition of the peripheral arterial walls at this entry. You will note that the pulse "wall was not felt." In view of the subsequent changes in the arteries it is well to bear this in mind. In passing, it is worth mentioning that the radial artery is no true index of the degree of an arteriosclerosis even in the peripheral vessels. The brachial, as a rule, shows a more advanced process. Perhaps if we examined the femoral or the popliteal more often we would find that these show a still more advanced degree of sclerosis.

The most important things to note in the laboratory findings are that the urine was negative and that the phthalein excretion was normal. In spite of these facts the diagnosis of chronic nephritis was made at that time. In 1914 and even later it was customary to consider all patients with hypertension, especially if the diastolic pressure was over 110 mm., as cases of chronic nephritis. We now know that this is not right, and that a large proportion of cases of hypertension even when there is

an accompanying albuminuria never have or never will have nephritis. The patient under discussion is such a case. It is now our custom in dealing with cases of high pressure, albuminuria, and cylindruria (hyaline casts only) to refrain from making the diagnosis "chronic nephritis with hypertension" until there is some diminution in renal function. This, of course, is not absolutely correct, because our tests for renal function are not delicate enough to detect the beginnings of what is to be a progressive chronic nephritis. However, it is by far the most generally useful procedure. In view of the probable circulatory origin of most of these chronic nephritics of the hypertensive type, in view of the interruptions that take place in the progress of the lesion, I wonder whether or not more delicate tests of renal function would help us much.

The patient entered the hospital for the second time on the surgical side on April 7, 1915. She was discharged May 20, 1915, after having had three operations. Two were for hallux valgus and one for a ventral hernia. The course in the hospital was uneventful. Two things only warrant comment. One is that the urine for the first time showed albumin and a few casts on one examination. The second fact worthy of comment is that all three operations were performed under local anesthesia due no doubt to the mistaken diagnosis "chronic nephritis." Local anesthesia is, of course, preferable to general anesthesia in all cases where the operation can be performed as successfully and as comfortably as under the general anesthetic. In the nephritic it has seemed to me that the surgeon has been over-cautious at times in refraining from using ether. My experience has led me to believe that if the patient's renal function is good that ether given in not too large a dose produces only a slight and temporary disturbance of the kidney. Of course, prolonged postoperative vomiting with abstinence from food and liquids may aggravate the kidney much more. On the whole, one may say that with a good renal function, other things being equal, one may operate under ether anesthesia with the expectation of getting only a slight and temporary irritation of the kidneys.

After these operations the patient dropped from sight for

almost two years. She entered the hospital for the third time January 29, 1917. She remained till March 1, 1917. This entry was for definite cardiac symptoms. For two years she had had an unproductive cough. About a month before this entry, after a cold, the cough had become worse. With this excessive coughing there developed a sharp, substernal pain. There was also noticeable throbbing in the chest and at times a rapid heart action. There was no headache or other symptoms.

Physical examination at this time showed certain definite changes in comparison with the first entry. The systolic pressure, 216, was not very different from that in 1914. But the diastolic was considerably higher, 149. The radial vessels had just begun to show slight thickening. There were, too, definite signs of change in the heart. No comparison of the size of the heart at this time and at the first entry could be made because, you may remember, in the earlier period the borders could not be made out. At this entry in January, 1917 the heart showed moderate enlargement. The apex impulse could just be felt 10 cm. from midsternum in the fifth space. The left border of dulness measured 12.5 cm. from midsternum and the right border 3.5 cm. The heart action was regular and only slightly above normal in rate. The first sound was everywhere soft in contrast to the second sound, which was sharp and clear, especially at the base. The first sound was accompanied by a soft murmur which could be heard all over the precordium, loudest in the aortic region from which it radiated upward into the neck. As you notice, auscultation at this time gives us a considerably different impression of the heart. The first sound has changed from one "of marked intensity" to one that is "soft," indicating myocardial weakening. The systolic murmur, which formerly could "just be heard" at the base, now has its point of maximum intensity in the aortic area and is transmitted upward. This is of interest because almost all of our hypertensive cases develop, sooner or later, a diffuse dilatation of the arch of the aorta made out chiefly by x-ray. In a large percentage of those developing such dilatation a systolic murmur develops, frequently rough in character, with point of maximum intensity

in the aortic area and transmitted into the neck and all over the precordium. There is no accompanying thrill or other signs of aortic stenosis and we attribute it to the dilatation and roughening of the aorta. Let us watch the changes taking place in this murmur. A word or two about heart sounds is in order at this point. Too little attention is being paid to the character of the sounds and much can be learned from noting their character. All soft first heart sounds obviously do not mean myocardial weakness. A thick chest wall may produce a soft first sound. But it must be borne in mind that such a thick chest wall must also decrease the intensity of the second sound at the same time. A contrast between the two sounds at the apex is important, therefore, in estimating the value of the cardiac first sound. Furthermore, if one observes what we have observed in this case, a cardiac first sound which has softened under observation, we can feel sure that a progressive weakening of the myocardium has taken place. Of course, other signs and symptoms may indicate this, but one should not neglect the value of such a change in sounds.

x-Ray examination of the heart showed a transverse diameter of 15 cm. and an aorta which measured 6.5 cm. The heart was not enlarged to the right.

Retinal examination was said to be "normal," although I am inclined to believe that the retinal arteries must have shown some sclerosis. As a rule these vessels are much further along in the sclerotic process than the peripheral vessels.

During the patient's four and a half weeks' stay in the hospital she improved markedly. Her symptoms disappeared and her blood-pressure fell in eighteen days from 216 systolic and 148 diastolic to 150 systolic and 100 diastolic. This was under rest in bed and a "low protein diet." I am inclined to think that the rest was the important part of the treatment. Certainly we know that the lowering of the protein in the diet plays very little part, and in this particular diet the salt is not materially decreased, 4 grams being served in twenty-four hours.

During the patient's stay in the hospital she received mercury

injections and KI till her mouth became sore. The mercury had no apparent effect on the kidneys. In fact, there was very little evidence of any chronic nephritis. Soon after leaving the hospital the patient's dyspnea began to return, and it was not long before she had to rest frequently while walking. After a few days of hard work she began to have severe precordial pain radiating down the right arm and occasionally down the left. Once in a while the patient felt "as if something in her chest stopped and then started again." This was undoubtedly an extrasystole with a long pause following it. The dyspnea became so great and orthopnea so troublesome that on June 11, 1917 she returned to the hospital.

Examination at this time showed that the heart was about the same size except that the supracardiac dulness seemed to have increased from $6\frac{1}{2}$ to 8 cm. There was definite precordial tenderness, a not uncommon finding in such cases. The action was regular and slow. The sounds were said to be "good" and the aortic second sound was markedly accentuated. The systolic murmur had not changed. The lungs were clear. The liver edge was somewhat tender and there was slight edema of the ankles. The blood-pressure had jumped back to 230 systolic and 130 diastolic. The vessel walls were now easily palpable, showing a definite increase in their sclerosis in six months. The urine showed the slightest possible trace of albumin and a rare cast. The phthalein excretion was 33 per cent. in two hours, ten minutes. This depression was possibly cardiac in origin, because it later was determined to be 60 per cent. A two-hour renal test was also normal.

The patient stayed in the hospital six weeks. Under rest in bed and digitalis the pains became less severe, but still persisted in lighter form. Two doses of diarsenol and much KI were given without any apparent beneficial effect and with no detrimental effect on the kidneys.

It is of great interest to note that the blood-pressure again fell sharply under rest. Despite the fact that the patient was on "house diet," with as much salt as she wished, her pressure dropped in nine days from 230 systolic and 130 diastolic to 140

systolic and 96 diastolic. She was discharged with a pressure of 156 systolic and 106 diastolic.

After leaving the hospital the patient went to a convalescent home and was quite well. She kept a supply of nitroglycerin on hand constantly, and a small dose usually relieved any precordial pain or distress. The effect of nitroglycerin in some cases of angina pectoris is extraordinary. A patient who is having tremendous tightness under the sternum with great pain when given 0.0006 gm. of nitroglycerin under his tongue changes almost instantly from a man in agony to one who is very comfortable. The effect is almost as striking as the effect of adrenalin in asthma. However, this type of cardiac distress and the nocturnal dyspnea that sometimes is associated are practically the only indications for the use of nitroglycerin. It certainly is not indicated to reduce blood-pressure. It is not desirable, as a rule, and usually has no effect.

After leaving the convalescent home our patient went to work in a country place in southern New Hampshire. Because of the snow and the cold she was confined to the house and got very little out-door exercise. The latter is a very important mode of treatment for cases of heart disease and hypertension, and its lack is often followed by a relaxation of peripheral and cardiac musculature that makes for a poorer circulation in the heart and other organs. As a result of the lack of out-door exercise, coupled with a cold, our patient began to slip back.

During the early part of 1918 she reported frequently to our Renal Clinic and complained of a return of her dyspnea on exertion. She had much cough with more or less "bronchitis" during February and March, and occasionally there was some edema of the shins. This "bronchitis" might have truly been an infectious thing, but it is more than likely that the heart played a prominent part, especially in view of the edema of the shins. The usual finding in those "bronchitis" attacks in the old is a combination of an infection with a mildly pathogenic bacterium like a diphtheroid and an underlying soggy lung from cardiac back pressure.

During the early part of 1918 the pressure remained fairly

high, about 220 systolic and 140 diastolic. In April the patient entered the surgical side of the hospital for a repair of a ventral hernia. There was very little at this time worthy of comment.

In July she returned to the Renal Clinic complaining of much pain in the arms, back, etc., not so readily relieved by nitroglycerin. Dyspnea on exertion was marked. Occasionally she had been spitting up small amounts of blood. This we attributed to her heart. Perhaps, however, in view of the postmortem findings, tuberculosis may have played a part. The blood-pressure at this time was about the same—212 systolic and 130 diastolic.

In October, 1918 the patient reappeared at the clinic, stating that there was increased cardiac pain of a constricting character. There was, too, considerable dry cough. Physical examination showed no change.

During the first half of 1919 the patient came to the Renal Clinic only once. Her dyspnea and pain had continued. About once in six weeks she experienced attacks of extreme dyspnea, palpitation, and choking. Coincidentally there were sharp shooting pains over the precordium radiating down both arms and frequently up the left side of the neck into the left ear. The pain was very severe, but was very short and was relieved by nitroglycerin. The latter, however, always gave her a very uncomfortable feeling of fulness in the head. It is said by some that this disagreeable sensation can be avoided if you can afford to wait for a slightly slower effect than that produced when the drug is absorbed from under the tongue. I refer to absorption from the stomach. The distribution of the pain in these attacks is of interest. It is well to bear in mind that the pain of angina pectoris is not always radiated in the classical way into the left shoulder and down the inside of the left arm. It not infrequently travels into the neck and back and down the right arm. At times in our patient it was much more noticeable in the right shoulder and arm than in the left. Occasionally it leaves behind a hyperesthesia of the skin. The choking sensation and the sense of constriction felt in the neighborhood of the base of the heart is attributed by Mackenzie to a spasm of muscles in the

neck and of the intercostals simulating the spasm of the right rectus in appendicitis.

In June the patient came to the Surgical Out-door Department for an infected finger and was so dyspneic that she was immediately sent into the hospital. This time she stayed only a week. Examination at this time showed that the heart was definitely larger. The apex impulse was 12 cm. from mid-sternum; the left border was 13 cm., the right 3 cm., and the supracardiac dulness in the second space 8 cm. The sounds were not different from those heard previously, but the systolic murmur at the base was definitely rough. The second sound at the base was ringing. The radial vessel walls also showed changes in that they were more easily palpable. They were not yet, however, tortuous or beaded. The pressure was high at entrance—230 systolic and 130 diastolic. It fell before discharge to 194 systolic and 108 diastolic. This drop was far from as much as during previous entries, although allowance must be made for the somewhat shorter stay. A 7-foot plate of the heart, from which accurate measurements can be made, showed at this time definite left-sided enlargement of the heart and dilatation of the arch. An electrocardiogram showed left-sided preponderance, but no "spreading" of the ventricular complex or other evidences of myocardial disturbance. It is of interest to note this fact, that the patient had had for a considerable time signs of a well-marked myocardial disturbance, and yet there was no evidence of it in the electrocardiograms. Sometimes we get almost the opposite effect, fewer symptoms of a severe nature and yet marked changes in the electrocardiographic curves.

During this stay in the hospital the dyspnea disappeared, but the precordial pain continued more or less. The urine was negative except for a rare cast. A blood urea nitrogen gave us one of those doubtful figures, 22 mgm. per 100 c.c., which in the presence of cardiac symptoms we are likely to consider as due to the heart and not to the kidneys.

The glucose tolerance test was interesting to us at that time because we were finding sugar not infrequently in the urine of hypertension cases. This test done on our patient showed that

she could not handle glucose taken by mouth nearly as well as she should. This is of interest because she had not been one of those cases that had previously showed sugar. Yet during the rest of her life this lady did show a glycosuria occasionally.

During the summer of 1919 the patient came to the hospital only once. She was working as housekeeper, cook, etc., and did real hard work in spite of the fact that her cardiac symptoms continued. Frontal and occipital headaches became more frequent. In addition, she developed other vascular symptoms, dizziness, sleeplessness, great nervousness, and irritability. Examination of her heart in July, 1919 showed no special change. The pressure was back at 226 systolic and 130 diastolic. The urine for the first time showed sugar.

In October the patient reported to us again. Because she had to work hard her symptoms were increasing. Precordial pain now came on every day, and at times was only relieved by nitroglycerin 1.5 mgm. She had been on digitalis in small doses most of the time. The urine showed a very slight trace of albumin, but no casts. Sugar was present. The phthalein excretion and blood urea nitrogen were normal.

In the first four months of 1920 our patient came to the clinic twice complaining that, if possible, the cardiac pain was even worse. In addition, the noises in her ears which she had had for years had become more prominent. There was also more or less edema of lower shins all the time.

In May, 1920 the patient entered the hospital again for her angina and stayed there about eight weeks. The heart at entrance was perhaps a bit larger and the supracardiac dulness was greater, too. x -Ray confirmed the greater dilatation of the arch. The first heart sound was of poor quality. Electrocardiograms showed nothing new. The urine was negative except for a slightest possible trace of albumin on one occasion. The blood-pressure was lower than at previous entries. However, in a few days it was 240 systolic and 165 diastolic, and continued high during this stay, in contrast to former entries.

During the first six weeks of the patient's stay, in spite of rest in bed, digitalis and nitroglycerin, with the addition of

potassium iodid and mercury rubs, the angina continued with but little change. In the last two weeks, however, this practically disappeared.

It was thought that possibly diarsenol treatment might be of benefit, and during the fall of 1920 the patient was given six intravenous treatments. Apparently the cardiac pain was not immediately affected. At any rate we know that there was enough pain to cause her to use up 100 tablets of nitroglycerin (0.3 mgm.) in a month. It is of interest, in view of her supposed nephritis, that the arsenic in no way affected her kidneys.

In November when she returned to the clinic there was a suggestion of pulsus alternans. In December she reported that she had had but one severe attack of angina. This was "terrific" and "lasted two hours." One should always bear in mind coronary thrombosis and infarct in these prolonged attacks of pain, especially if they are not relieved by nitrites. This attack was particularly interesting in that it came on about three hours after a long walk. It is difficult to explain these delayed attacks of angina.

It is of interest to note that retinal examination on December 1st showed moderate sclerosis of the retinal arteries, a hemorrhage in one eye and "white spots" in the other. This apparently was a warning of what was to come. The urine at this time was normal except for sugar and the functional tests were all normal.

Shortly after the middle of December she rather suddenly began to have a profuse vaginal discharge, as if an abscess had ruptured into the vagina. Examination later disclosed no such opening. The irritating, non-productive cough became worse. The patient was no longer able to work because of her heart and was very uncomfortably situated in her daughter's home. On January 5, 1921 her blood-pressure was found to be 248 systolic and 120 diastolic. Because of all of the above factors it was thought desirable to admit her again to the hospital until we could make arrangements for her in a chronic hospital.

The patient entered the hospital for the last time on January 6, 1921, and stayed here until her death February 23, 1921. At entrance she showed emphysema of the lungs, which is not

unusual in the elderly and in the chronic vascular cases. The heart was not different apparently than at former entries. The radial vessels were very easily palpable. Curiously enough, the blood-pressure was lower—185 systolic and 135 diastolic—which lowering did not seem to be due to an increased weakness of the heart muscle.

During her stay in the hospital the precordial pain persisted and was relieved much by nitroglycerin, which she kept with her constantly. Occasionally the pain was so severe that the nitroglycerin did not give her entire relief. The blood-pressure varied from 185–215 systolic and 100–135 diastolic. The urine showed no change. From her multiplicity of symptoms we gradually gathered that the patient was exaggerating somewhat, lest she be sent from the hospital. An attempt was made to get her into a chronic hospital, but without success. About February 20th it was decided that we could not do anything more for her and that she was as fit as she was going to be. Further stay did not seem warranted. On February 23d she was told that she must go home. At this she became very much excited, especially during the preparation. She seemed, however, to be in good condition. She walked to the toilet and was found there shortly afterward dazed and pale. Forty-five minutes later she was more dazed, complained of headache, and showed a flaccid paralysis of the left arm and leg. Later she developed conjugate deviation of the eyes to the right, which did not persist. In the afternoon she gradually became comatose and died at 8.30 P. M.

At autopsy, which we were especially fortunate to get, many interesting findings were made. The aorta was moderately dilated and showed also two out-pocketings in the left lateral surface of the arch. These were small, about 1 and 2 cm. in diameter, and the walls were definitely calcified. The aorta throughout its length showed considerable atheromatous change. There was much calcification, especially in the region of the arch. The coronary arteries disclosed only a "moderate amount of atheromatous thickening in the main branches, and no occlusion or thrombi." The small amount of disturbance in the coronaries

is indeed surprising in view of the severity of the angina. It bears out, however, the theory that it is not the coronaries alone that are responsible, but that the pain comes from the muscle itself. The coronaries by their lack of distensibility carry an insufficient supply of blood to the muscle when the latter is overworking and calling for an increase. The heart muscle showed more or less fibrosis macroscopically and microscopically. The right heart was somewhat dilated. The left ventricular wall moderately hypertrophied. The cusps of the aortic and mitral valves were somewhat thickened. It is possible that this thickening of the aortic valve may have played some part in the roughness of the basal systolic murmur. It is more likely, however, that the roughening and dilatation of the aorta played the greater part.

The kidneys are of great interest in view of the original diagnosis of chronic nephritis. Each weighed 165 grams. The capsule stripped easily from a smooth, red surface. On section, the kidneys were normal. The larger vessels showed much arteriosclerotic thickening. The small arteries did not seem abnormal. Microscopically, however, they did show definite sclerotic change. Under the microscope there was considerable distention of the capillaries between the tubules and in the tufts. An occasional glomerulus showed some thickening of the capsule, but there was absolutely no suggestion of the so-called "chronic interstitial nephritis" that was diagnosed in 1914.

In the brain there was a fairly large hemorrhage into the right lateral ventricle.

A peculiar finding was made in the mediastinum. Closely approximated to the trachea and bronchi on either side was a firm, dark red mass about 3 x 3 x 5 cm. The one on the left extended into the neck. At first they suggested tumor masses. Frozen sections of these showed miliary tubercles, and an emulsion of a part of a gland injected into a guinea-pig produced a growth of tubercle bacilli.

This case, as you see, illustrates many phases of the problem of vascular disease. A woman beyond middle life is discovered to have a positive blood Wassermann. She is sent into the

hospital for lumbar puncture, and on the basis of her hypertension she is diagnosed chronic nephritis. During the next seven years her symptoms have been largely cardiac. In addition, she developed under observation an inability to handle sugar and was at least a potential diabetic. And yet she died from a cerebral hemorrhage and autopsy showed no nephritis. Truly, prognosis as to the time and the type of death in vascular disease is hazardous.

CLINIC OF DR. EDWIN A. LOCKE

BOSTON CITY HOSPITAL

SYPHILIS OF THE LUNGS

WE have for discussion today a case of unusual interest from the point of view of diagnosis, and one which is fairly typical of a very important disease.

Male of sixty-five, first seen March 5, 1921.

Family History.—Father died at seventy-nine of pneumonia. Mother living and well at eighty-three. One sister died when patient was a very small boy, cause unknown.

Past History.—The patient has always been unusually robust, and recalls only one serious illness, namely, typhoid fever at thirteen. He has never been subject to colds or bronchitis. His usual weight has been 170 to 175 pounds; six months ago it was 165 pounds.

About fifteen years ago the appearance of a general macular rash led him to consult a specialist in Boston, who made a diagnosis of secondary lesion of syphilis. He was given a vigorous course of treatment with mercury and potassium iodid, and no symptoms developed until a few years later, when lesions in the septum and turbinates appeared. These were diagnosed as due to lues. About the same time the left knee became slightly swollen, stiff, and moderately painful. The patient at this time again underwent a long and vigorous course of treatment with mercury and iodids, with entire relief of the symptoms just described. He considers that he was entirely well until the fall of 1919.

Present Illness.—Some time in September or October of 1919 he noted the gradual onset of symptoms of moderate pressure across the front of the chest with slight limitations in breathing. A few weeks later he began to have a troublesome

cough, which at the end of a few months became paroxysmal in character and was diagnosed as whooping-cough. In January, 1920 the symptoms just mentioned had become so severe that he was obliged to give up work. He consulted a physician, who found signs in the chest which he interpreted as those of fluid, and suggested the possibility of pulmonary tuberculosis. Paracentesis of the chest yielded only a few cubic centimeters of clear straw-colored fluid. The cough and dyspnea increased gradually in severity, he lost in weight and strength, and was finally confined to the house. By February 1, 1920 he was obliged to go to bed. It was at this time that a diagnosis of probable syphilis of the lungs was made. The signs in the chest at this time are not known. The Wassermann test was + + + +. Three doses of salvarsan were given at ten-day intervals, with marked relief of the symptoms. Following this treatment the Wassermann remained + + + +.

In May, 1920 three more doses of salvarsan were given. In July, 1920 the Wassermann was still + + + + and a very vigorous course of treatment with potassium iodid was carried out for several months and followed by inunctions of mercury, without, however, any striking benefit. A fourth Wassermann test made in October, 1920 was + + + +. He was then given arsphenamin, one dose every seven days for eight weeks, but in spite of this the Wassermann remained + + + +.

Since October, 1920 the general condition has remained about the same. The chief symptoms have been the increasing dyspnea with exertion, marked prostration, and excessive cough. The cough has continued of the same character, but the paroxysms have been more severe and frequent. They are especially intense in the early morning and on going to bed. Vomiting has occasionally resulted from the severe cough. He has noted some wheezing and rattling in the chest. As a rule the sputum is very scanty and usually raised only at the end of a prolonged and strangulating coughing attack. During the entire twenty-four hours only an ounce or two of mucoid, stringy material is raised. It has never been purulent or bloody. Repeated examinations for tubercle bacilli have been negative.

There has been no pain in the chest. The shortness of breath is so extreme that even slight exertion now produces a condition of complete breathlessness. No orthopnea. Anorexia has been a prominent symptom and, as a rule, he eats very little. As a result his nutrition has suffered greatly and his weight has dropped from 175 pounds, a year ago, to 129 pounds.

The temperature has always been normal in the morning, but occasionally has shown slight elevation in the afternoon, on one or two occasions reaching 102° F. The blood-pressure has always been found normal. The urine has shown no abnormality except a slight trace of albumin for some few months past. Never any jaundice.

Physical Examination.—Temperature 101° F. Pulse 100. Respirations 30.

A moderately emaciated, slightly pale old man who seems excessively weak. Respiration rapid, shallow, and labored, but no orthopnea. Frequent and very distressing paroxysms of cough, which are chiefly unproductive, and leave him in a state of collapse. The small amount of sputum which is occasionally raised is frothy and mucoid.

Only slight degree of arcus senilis. Pupils equal and react normally to light and distance. No enlargement of the lymph-glands. Teeth largely false, the remaining ones well cared for. Throat somewhat reddened and tonsils seem normal. The superficial and deep reflexes are normal. The osseous system shows no abnormalities. The heart is normal in size and position, the action regular, sounds of fair quality, no murmurs. The arteries are soft and not tortuous. Blood-pressure 110/80. The abdomen is negative. The fingers and toes show a considerable degree of clubbing, but there is no evidence of any change in the size of the bones of the forearms or lower legs.

Lungs.—The thorax is very thin, but not deformed, except that it is slightly less full on the right side. Respiratory movements on the right are somewhat less than on the left. On percussion the upper portion of the right front seems slightly hyperresonant, but below the second rib the note is slightly dull. This area of dulness continues to the axilla, and in the

back takes on a much more definite character. Over an area in the right back extending from the spine of the scapula to just below its inferior angle the dulness is quite marked. Over the area of dulness and especially posteriorly the respiration and fremitus are of a quite intense bronchial type, with an added amphoric tone. Many medium and coarse crackling râles are heard over this same area. Throughout the entire chest there are a few scattered medium crackling râles. In the left back just below the spine of the scapula and over an area of 2 or 3 inches in diameter the respiration is distinctly bronchovesicular and the vocal fremitus is slightly increased.

Urine normal. Stools normal except for a moderate amount of mucus.

Blood count: Hemoglobin 70 per cent.; white blood count 15,000 per c.mm. The stained smear shows no abnormalities.

Wassermann test + + + +.

Sputum (several examinations) negative for tubercle bacilli.

x-Ray examination (Dr. Morrison): The diaphragm is high on the right and appears adherent. The right lung shows a rather dense lace-like fibrosis nearly throughout, but particularly from the hilus outward to comprise the middle two-thirds of the entire lung. The apex is fairly clear, showing only very slight mottling. The mediastinum is drawn moderately to the right by dense scar tissue which comprises the entire root of the right lung. On the left the apex is clear, but at the level of the second and third interspaces there is considerable thickening, and toward the base and spreading out from the heart is a quite dense infiltration. In the stereoscopic plates this fibrosis seems to be posterior. The heart is not enlarged or displaced. The general appearances in the lungs are typical of a chronic fibrosis such as is common in bronchiectasis. Its distribution is definitely peribronchial.

Subsequent History.—The patient remained at a private hospital for eight weeks under a general régime of rest and careful dieting. For the first few days the temperature was somewhat elevated (the maximum 101° F.), which the patient explained as due to a grippy cold which he contracted the day

before entrance. Subsequently the temperature never exceeded normal and the pulse ranged from 66 to 74. For the first thirteen days the respirations ranged from 30 to 32, then fell to normal, and have remained so.

The patient was given antisyphilitic treatment as follows: neosalvarsan at weekly intervals for eight weeks, beginning with 0.45 gram and increasing to 0.6 gram.

At first the improvement was exceedingly slow, but after the second or third week became much more rapid. All of the symptoms mentioned above abated and the general nutrition was greatly improved. At the end of his stay in the hospital (eight weeks) he had gained 28 pounds, his general appearance had improved very strikingly, the cough had largely disappeared, and the dyspnea was not noticeable. He was up and about from ten to twelve hours daily and was able to walk one or two miles without fatigue. He said he felt himself to be in better physical condition than he had been for many years.

Examination of the chest showed only moderate dulness on the right, where it had eight weeks previously been marked, and over this same area the changes in the respiration and fremitus were of a less definite character. A few crackles remained in the mid right back and an occasional râle was heard over the rest of the chest. Unfortunately, a second x-ray examination at the time of discharge was not made.

Discussion.—Differential Diagnosis.—To summarize the case, we have a man of sixty-five with negative past history except for a syphilitic infection fifteen years ago, who for a year previous to coming under observation in March, 1921 gives a history of the gradual development of intense paroxysmal cough practically without sputum, severe oppression in the chest, and shortness of breath with even slight exertion, only occasional and insignificant temperature, marked emaciation, extreme weakness, and signs of extensive infiltration in the right lung and slight in the left. During his stay of eight weeks in the hospital he received eight doses of neosalvarsan. At the time of discharge his symptoms were entirely relieved and his general condition showed a very extraordinary improvement.

Diagnosis in this case clearly lies between malignant disease, pulmonary tuberculosis and syphilis, but a positive diagnosis is much more difficult than would at first appear. The combination of cough and dyspnea which gradually increased to an extreme type and accompanied by progressive emaciation is in a general way very suggestive of new growth of the lungs. If present it seems probable that it must be primary in the lungs, as no evidence was found of neoplasm elsewhere in the body, and the extreme rarity of a primary disease of the lungs makes the diagnosis very improbable. The physical signs are consistent with new growth. The leukocytosis seen here is common to this condition. On the other hand, several features of the case are strongly against the diagnosis of neoplasm. The emaciation is without significance in differential diagnosis in this case, as it is as common to one as to another. Furthermore, it seems clear that it was in part at least due to the direct result of the severe anorexia which led to the ingestion of an insufficient amount of food. Furthermore, a gain of 28 pounds in two months while under treatment in the hospital is inconceivable were the patient suffering from cancer of the lung. Pain is a prominent and an almost constant symptom of pulmonary disease of this type and was never present in this case. No type of sputum can be said to be strictly characteristic of lung cancer or sarcoma. It may even be absent, especially in the early stages. At some time in the course of the disease, often throughout, blood in some form is apt to be present. The x-ray appearances are not such as I have ever seen in malignant disease of the lungs. If malignant disease had been present the x-ray would have shown a steady progression in the lesions rather than a retrogression. Finally, the course of the disease under treatment, namely, the marked gain in weight, the constant improvement in the patient's general condition, and very marked lessening of the pulmonary signs and symptoms, positively exclude new growth.

Tuberculosis likewise seems to me very improbable. It must be admitted that any chronic disease of the lungs accompanied by cough always suggests tuberculosis, and when one

meets such a combination of persistent cough with progressive loss in weight and strength with signs of infiltration in the lungs the diagnosis of tuberculous infection is even probable. Never forget that the disease is a very common one in very old people and almost always overlooked. Whenever you see an aged person who is thin and has a chronic cough, whether with or without fever and sputum, first of all give very careful consideration to the possibility of phthisis.

Many facts are definitely against the diagnosis of tuberculosis. The negative family history so far as tuberculosis is concerned is a point of no small significance on the negative side. Pulmonary tuberculosis, especially in the aged and of the fibroid type, may run an afebrile course, but is most unusual. The fact, then, that this patient has had no significant elevation of temperature except for a few days at entrance to the hospital when he was suffering from a grippe-like attack seems very inconsistent with a tuberculous process. Similarly, it is hardly conceivable that disease of this type in the lungs should progress to the stage of producing such extreme symptoms without considerable increase in the pulse and respiration rate. A marked leukocytosis except with complications is never seen in tuberculosis of the lungs. When taken with other negative evidence the persistent absence of tubercle bacilli in the sputum is important also. The process in the chest is very atypical of tuberculosis both as regards its character and location. The apices are free of disease. Likewise the x-ray appearances are not such as are commonly seen in this disease. Improvement in the general nutrition and in the symptoms and signs might result from the rest in bed and forced feeding, but it would be most unusual to have these changes come about so promptly and so strikingly, particularly in a man of sixty-five. While I feel that one cannot absolutely exclude tuberculosis, it seems to me highly improbable that it is the chief infection. In the presence of some other disease one must admit, I think, the possibility of the presence of tuberculosis as a complication.

A close study of the case with reference to the possibility of syphilis of the lungs brings out several points of unusual

importance which I wish to emphasize. It has been frequently observed in this disease that the signs in the chest are much more striking than the symptoms. The onset is so insidious and slow that only very moderate symptoms are present when extensive infiltration has taken place in the lungs. In this respect this case, if the process in the lungs is syphilis, does not conform strictly to the general rule. Furthermore, the extreme degree of prostration and loss in weight is very atypical except in the very late stages of the disease. On the positive side the man was known to have syphilis. We have failed to prove the presence of tuberculosis, and, in fact, the evidence as presented above is, on the whole, against such a diagnosis. The intense form of dyspnea and the persistent paroxysmal cough are much more common in syphilis than in tuberculosis. Temperature was practically absent, which is much more often the case with the former than the latter. The leukocytosis is common in specific disease of the lungs. No type of changes shown in the roentgenograms of the lungs can be said to be characteristic of lues, and yet those shown in this case are such as are often seen with this condition and almost never with tuberculosis. Most important of all, the improvement not alone in the symptoms and general condition of the patient but also in the physical signs was so emphatic as to constitute almost positive proof of a syphilitic infection. While absolute proof is lacking, the evidence which I have just given you seems to leave but little reason for doubt that we are dealing with a true example of syphilis of the lungs.

I shall now attempt to give you a brief summary of what is known regarding syphilis of the lungs as it occurs in adults.

Frequency.—One is first of all impressed by the apparent rarity of the invasion of the lungs in syphilis, and, furthermore, that a positive diagnosis is much more often made in the wards than in the postmortem room. On the question of the frequency with which the lungs are involved in lues there is an extraordinarily wide difference of opinion. Many clinicians as well as pathologists hold that this type of disease of the lungs is excessively rare. Many statistics might be quoted in support of

this opinion. In this hospital, for example, among 4265 autopsies no instance of syphilis of the lungs has been found. Similarly none were found among 3000 postmortem examinations at the Massachusetts General Hospital (Lord), and only 12 among 2800 necropsies at the Johns Hopkins Hospital (Osler). McCrae and Funk (Jour. Amer. Med. Assoc., 1919, xcvi, 600) found only 4 cases of undoubted syphilis of the lungs among 1200 cases referred to the Jefferson Chest Hospital for pulmonary tuberculosis. On the other hand, a considerable group of writers contend that the disease is by no means an uncommon one. Lisser, who has recently published an important paper on the subject (Amer. Jour. Med. Sci., 1918, clv, No. 3, 356), discusses this question at some length, and suggests that the rarity of syphilis at the autopsy table is "due in part to the failure of the pathologist to recognize syphilis." He particularly emphasizes the fact that it is exceedingly difficult to differentiate between syphilis and tuberculosis of the lungs both clinically and pathologically. There seems considerable evidence that even in the autopsy room syphilitic lung lesions are usually mistaken for those of tuberculosis. The pathologist demands proof of the syphilitic nature of the lung lesions by the demonstration of the presence of the *Spirochæta pallidum* which is seldom possible. Lesser quotes Virchow as saying "some patients die of so-called tuberculosis for lack of antisypilitic treatment." Carrera, in an important paper recently published (Amer. Jour. of Syph., 1920, iv, 1), gives the results of his study of 152 cases of syphilis studied at autopsy. Among these he found 12 cases showing unmistakable lesions of syphilis in the lungs. This author concludes that, contrary to the general belief, "the lungs are involved in the mild infections of syphilis to about the same degree that the other organs and tissues are." Furthermore, he finds that the lesions in the lungs are essentially the same as in other organs. In the routine of postmortem examinations but a small portion of the lungs is examined, and in consequence the tissue changes due to syphilis are often overlooked.

The opinion of the majority of the most recent writers on the subject is that secondary syphilis of the lungs while a rela-

tively rare condition is by no means so unusual as was formerly supposed. Patients do not die of the disease, hence the diagnosis must be essentially a clinical one. Pulmonary lesions in syphilis usually develop only after a period of several years, occasionally as late as fifteen or twenty years.

Pathology.—So much has been written of late years on the pathology of pulmonary syphilis and the types of lesions described are so varied that it is difficult to give a simple classification. Anatomically the most important and common lesions fall into two general groups: (1) gummata and (2) diffuse fibrosis. Both types of lesions are often associated. The gummata may be single or multiple, vary from a minute size to 10 or 15 cm. in diameter, and may be caseating or non-caseating. Caseation most commonly occurs in those of large size. Their location is varied and there is no special predilection for any particular portion of the lung, as is so often stated, although they are perhaps somewhat more frequently found at the root of the lung and in the lower lobes. In general appearance and structure the small gummata closely resemble tubercles and are often mistaken for them. The pathologic picture is complicated by a variety of changes in the different tissues, including inflammatory reaction in the area about the gummata, necrosis, arteritis of the large vessels, peribronchial fibrous infiltration, and calcification. With breaking down of the gummata cavity formation may result, or more commonly the production of a puckered scar and dimpling of the lung surface when healing occurs. If in connection with a bronchus the former process sometimes leads to the development of bronchiectatic cavities.

When the syphilitic process takes the form of diffuse induration or fibrosis a quite different picture results, usually ending in a generally deformed and sclerosed lung. The lung is intersected by long strands of connective tissue following along the bronchi and blood-vessels and radiating from the hilus. This process is generally unilateral. At times the connective tissue formation takes the form of patchy fibrosis scattered throughout a lobule or lobe. Bronchial stenosis has been

observed. Kokawa (*Arch. f. Derm. u. Syph.*, 1906, lxxviii, 69 u. 319), as a result of a careful histologic study of these lesions, says that the process begins in the perivascular tissue and later passes into the interlobular, peribronchial and inter-alveolar tissues, and even the pleura. Carrera concludes from his histologic investigations that the gumma, fibrosis, peribronchitis, and arteritis constitute a specific syphilitic pathology.

This author found a terminal broncho- or lobar pneumonia in a large percentage of the cases examined and believes the condition is associated with a failing heart. Levaditi (*Annale de l'institut Pasteur*, 1906, xx, 41) reports the finding of spirochetes, often in great numbers, in most cases. They were chiefly in the bronchi, but also in the lung tissue, capillaries, and alveoli. It is usually considered as an extremely difficult organism to demonstrate in the lung tissues.

Symptoms.—No symptoms can be considered as characteristic or distinctive of lung syphilis, those commonly described being general to any inflammatory disease of the lungs.

The onset is always insidious and the progress of the disease very slow. Until the syphilitic process in the lungs becomes extensive and advanced no symptoms may appear. It is usually only when this stage of the disease is reached that symptoms of general intoxication, anorexia, loss of weight and strength, anemia, etc., are evident.

The two most common symptoms are cough and dyspnea, but neither have any characteristic features. The cough is at first dry and irritative and may remain so, or later a moderate amount of greenish-yellow sputum may be raised. In many instances the cough is of the severe paroxysmal type, as in the case which we have just considered. The sputum rarely becomes purulent and fetid. Hemorrhage is infrequent, but may be profuse, and fatal hemoptysis has been recorded. Dyspnea bears a direct relationship to the extent of the lung fibrosis. It is a common symptom and occasionally is very intense and spasmodic. A moderate degree of fever is characteristic of the late stages of the disease, but, as a rule, in its early course the patient is afebrile. Janeway (*Trans. Assoc. Amer. Phys.*, 1898, xiii, 23)

has particularly called attention to the fact that fever is one of the common manifestations of visceral syphilis. Night-sweats are very apt to occur during the period with pyrexia. Pain is very rare.

As in the case of the symptoms, the physical signs of pulmonary syphilis are in no respect distinctive. The most important consideration is that it is quite characteristic for the physical signs to be out of all proportion to the symptoms. A slight cough and dyspnea may be the only symptoms to correspond with very extensive signs in the lungs. The signs in general may be said to be those of pulmonary tuberculosis, though they are much more apt to be unilateral.

Diagnosis.—The greatest obstacle to the diagnosis of this condition is the usual absence of striking symptoms to direct attention to the lungs. One should always keep in mind the possibility of invasion of the lungs in every case of tertiary syphilis. As the symptoms and signs are not characteristic, the diagnosis is very often made only by exclusion. Indeed, it is frequently impossible to establish the diagnosis positively until the postmortem examination.

Several considerations are of especial importance in diagnosis.

1. It is necessary to establish definitely that the individual has syphilis. Symptoms are not diagnostic of lung syphilis, but a carefully taken history with reference to the presence of the disease in other parts of the body should be obtained. The evidence of syphilitic infection must be undoubted. As a rule syphilis of the lungs does not occur without undoubted luetic lesions in other parts of the body.

2. The complement-fixation test is of less value than might at first be supposed. A positive Wassermann proves that the patient has syphilis, but not that the lesions in the lungs are necessarily due to this infection. The importance of this reaction comes to the front in those cases where all the evidences for tuberculosis are wanting. Do not forget that this test is sometimes negative in syphilis, and that, therefore, syphilis must sometimes be considered in spite of a negative Wassermann.

3. The sputum must be negative for tubercle bacilli, as the

signs in the chest may be equally characteristic of either tuberculosis or syphilis. The two diseases not infrequently coexist, however, and a sputum positive for tubercle bacilli cannot be said to rule out the presence of syphilis.

4. In the presence of a positive Wassermann or other unmistakable evidence of syphilis, signs of infiltration at the hilus or the base of the lung are always strong presumptive evidence that the pulmonary disease is of this origin. Landis and Lewis (*Amer. Jour. Med. Sci.*, 1915, ci, 195) have called attention to the possibility of focal lesions at the apex of the lung, which are obviously not tuberculous, being due to syphilis.

5. Do not forget that the x-rays seldom furnish us any certain criteria for differentiating syphilis from tuberculosis. The importance of the roentgenologic examination lies in the fact that both in the cases with gummata and those with fibrosis the x-ray often gives us a much more exact idea of the extent and type of pulmonary lesions than do auscultation and percussion.

6. One of the most important considerations in diagnosis is the therapeutic test. If the process in the lungs be due to specific infection a vigorous course of antisyphilitic treatment should yield very prompt and striking improvement in the symptoms, and except in the cases of advanced fibrosis in the physical signs as well. Neither malignant disease nor tuberculosis of the lungs show any evidence of being favorably influenced by the use of mercury and iodids or salvarsan.

Prognosis depends largely on the stage of the disease and the thoroughness of the treatment. If the disease has reached a late stage, with very extensive fibrosis, cavity formation, and bronchiectasis, very little improvement can be expected, although the progress of the disease may be arrested. In the less advanced types the response is often extraordinary, and complete cures have frequently been reported. The prognosis is most unfavorable in those with both syphilis and tuberculosis in a well-developed stage. The treatment is that of syphilis in general.

CONTRIBUTION BY DR. FREDERICK T. LORD

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A DISCUSSION OF THE DIFFERENTIAL DIAGNOSIS OF A CASE OF SPINAL TUMOR¹

THE following case history illustrates an uncommon and important neurologic problem. In the discussion I shall make use of the written criticisms of the record, the diagnoses, and therapeutic suggestions of forty physicians who have considered it.²

N. M. L. (193267 M., 199254 N., 203413 S., 257404 O. P. D.) Forty-three. Single. Born in Ireland, living in Massachusetts. Laundress.

Past History.—Measles, scarlet fever, and whooping-cough as a child. Otherwise well.

Family History.—Father well. Mother "paralyzed." Two brothers and 4 sisters well.

Habits.—Tea 3 to 4 cups. Coffee moderate. Alcohol only rarely.

Catamenia.—Regular. not painful. Scanty for two years past.

Present Illness.—About twenty-two months ago she noted that she was clumsy on her feet, but paid little attention to it. About this time she had a backache one night severe enough to keep her awake for part of the night. The next morning her back

¹ Presented May 6, 1921, as part of a series of eight exercises at Pittsfield, Mass., under the auspices of the Harvard Medical School Courses for Graduates. The case of "epidural intraspinal tumor of two years' duration; operation; recovery," has been reported by Dr. W. E. Paul, Boston Med. and Surg. Jour., vol. clxxv, No. 4, pp. 153, 154, July 27, 1916.

² In Dr. Lord's course for graduates in Physical Diagnosis and Medical Practice at the Massachusetts General Hospital.

had ceased to trouble her, but the clumsiness was more apparent and the feet felt numb. When walking she would stumble and fall and had difficulty in raising her feet over the curbing. She could put her left foot into very hot water and stick pins into it without any sensation. In the course of the next two months the numbness had extended somewhat up the left leg. The right foot and leg were less affected than the left and the prick of a pin and temperature sense could be appreciated, but the leg was weak.

During the succeeding nine months there was increasing stiffness of the legs and greater difficulty in getting about, especially in getting on and off cars. The numbness has extended until it now involves almost the entire left leg, but is confined to the region between the toes and the inner aspect of the leg on the right.

About a year ago she began to have an uncomfortable dull ache, lasting one day at a time and coming every few weeks in the upper lumbar region. She has had a sense of constriction about the abdomen. The feet and legs at times feel very hot, at other times very cold, and there has been a sensation in the arches of the feet as if she were standing on something firm. The disability has slowly increased so that she is unable to do even light work because she can't stand. Ordinarily she can get about by supporting herself on chairs or tables, but she walks very stiffly. During excitement she can neither stand nor move the legs.

For some months the bowels have been either loose or costive and she occasionally has an involuntary stool after the use of a cathartic. The urine is either hard to start or comes too readily and is occasionally involuntary. No night urination.

At times the feet have been slightly swollen at night.

No pain other than that mentioned. No tenderness. Fair appetite. Occasional sour stomach. No gas or vomiting. No dyspnea, cough, or expectoration. No loss of weight or strength.

Physical Examination.—Well developed. Obese. Skin and mucous membranes good color. Pupils: L. greater than R., reg-

ular outline, round, react to light and distance. *Fundus*: Opaque nerve-fibers o. u. Old changes in macular region o. d. Upper teeth false. Many lowers missing and some carious. Tongue not tremulous, protrudes in middle line. No lead line. No glands. *Heart* impulse palp. fifth space nipple line, 12 cm. to left of mid-sternum. Right and upper border o. k. Slow, regular, good quality. P^2 greater than A^2 . Soft systolic murmur at apex. *Pulses* regular, good volume. *Spine* negative. *Lungs* negative. *Abdomen* full, soft, tympanitic. No masses. Liver, spleen, and kidneys not felt. No costovertebral tenderness.

Slight varicosities of the veins of both legs. Very slight edema of the lower shins.

The patient was first examined twenty months ago, and again eight months ago. The results of these and the present findings may be summarized as follows:

Reflexes.—Biceps, triceps, and periosteoradials somewhat increased and equal. Abdominal reflex not obtained. Both knee and Achilles' jerks exaggerated, the right knee-jerk being greater than the left. Ankle- and patellar clonus both sides, the ankle-clonus being greater on the right. Marked Babinski on the right. Left plantar reflex normal. Gordon and Oppenheim reflexes variable, at times present on the right, absent on left.

Sensation.—At the first examination the sense of touch was everywhere unimpaired, but there was diminished pain and temperature sense throughout the left leg, the left thigh, and the left gluteal region. Eight months ago there was impairment of the sense of touch in both lower extremities and the trunk as far upward as the lower borders of the thorax. At this time pain and temperature sense were disturbed over this entire area, but, contrary to the first observations, pain more markedly on the right than on the left, while the temperature sense was more disturbed on the left, as before.

At present the sensory dissociation has progressed to marked impairment of touch and almost complete loss of appreciation of heat, cold and pain over both lower extremities and the trunk as far upward as the nipples in front and the angles of the

scapulæ behind, sharply limited above. Joint and muscle sense lost in legs. No atrophy. No muscular twitchings. Tremor of extended fingers. Romberg present even with eyes open. Staggering spastic gait. Some impairment of motion of legs, the flexors and extensors of the right being weaker than those of the left leg.

Blood-pressure 160 systolic, 85 diastolic.

Temperature normal. Pulse 80. Respiration 20. Urine negative. Luetin test negative.

Blood.—Wassermann negative. Whites 7000. Hgb. 85 per cent. Neutrophils 69 per cent., lymphocytes 29 per cent., eosinophils 1 per cent., mast cells 1 per cent. Reds negative. Lumbar puncture (three investigations), clear fluid. Pressure 150 eight months ago and 210 mm. Hg. now. One to 8 cells, of which 60 per cent. were neutrophils and 40 per cent. lymphocytes. Wassermann negative (three trials). Noguchi, Nonne, and alcohol test all positive. Lange's colloidal gold chlorid test twenty-two months ago "pathologic, but negative for syphilis," eight months ago "syphilis," now "syphilis or non-tuberculous inflammation."

x-Ray of spine negative.

DISCUSSION

The first matter for consideration is whether there are any further data in the history which should be known, and in the replies a few have asked whether or not there are speech defects, nystagmus, or mental or visual disturbance. Of these there were none. A statement regarding them should have appeared and their omission is a justifiable criticism. The present illness should also include an inquiry into the function of the cerebrum, cerebellum and cranial nerves, and at least a statement made regarding the presence or absence of any symptoms of intracranial disturbance. With these exceptions the history is to be commended as an adequate presentation of the progress of the illness. I have already dwelt on the importance of presenting the evolution of symptoms in diagnosis in general. In neurologic problems the evolution of symptoms is especially significant in

processes starting as focal lesions of the brain and spinal cord in the progress of which the original site is masked by irritative, compressive, or destructive phenomena. Thus in focal lesions of the upper motor segment there may be initial localized muscular contractions involving one group of muscles and followed by the involvement of other groups, with finally a unilateral or general convulsive seizure. Sensory phenomena may initiate or accompany the attack, and weakness of the muscle group first affected is likely ultimately to follow. Such a complex is spoken of as cortical or Jacksonian epilepsy. If the march of events is unheeded it is likely to result in failure in the localization of the process.

Regarding the physical examination little comment is necessary. The opaque nerve-fibers in both eyes are due to medullated nerve-fibers in the retina, a congenital anomaly. Further details are desirable regarding the change in the macular region in the right eye. The neurologic examination may be criticized as not sufficiently complete. A statement should have been included indicating that the function of each cranial nerve had been tested and questions asked and tests applied to determine any evidence of disturbance in the cerebrum and cerebellum. The establishment of a disturbance within the cranial cavity in this case might completely change the recommendations regarding treatment, and as the record stands we can only assume that intracranial disturbance is lacking. Some have asked for the electric reactions. They are of diagnostic value when there is a question between lower and upper motor segment paralysis. The reaction of degeneration in which there is no muscular response to faradic and a characteristic slow response to galvanic stimulation indicates a disturbance in the lower motor segment, but the absence of atrophy and the presence of the tendon reflexes are sufficient to exclude lower motor segment paralysis here without resort to electric tests.

Passing to the question of differential diagnosis, let us consider this aspect of the case by discussing the diagnoses made. Twenty of forty physicians apparently regarded the condition as due to syphilis. To be more specific: Six made a diagnosis

of *tabes dorsalis*, thus classifying the disturbance as a degenerative process affecting the sensory system and due to syphilis, 3 made a diagnosis of cerebrospinal or spinal syphilis, 6 of ataxic paraplegia for which antisyphilitic treatment was recommended, 2 of syringomyelia with similar advice as to treatment, 2 of syphilitic myelitis, and 1 of syphilitic growth. These are interesting conclusions and raise the question as to how far reliance can be placed on clinical and laboratory data in the exclusion of syphilis.

Even the most obscure cerebrospinal syphilis usually presents suggestive clinical manifestations, such as pains which fail to conform to the usual type in other organic diseases, and fall into the group of gastric, rectal, or other crises, nausea and vomiting out of proportion to the severity of the pain, girdle sense, irritability, failure of memory, attacks of unconsciousness, disturbances of hearing or vision, difficulties with urination, etc. Physical examination is likely to show irregularity, inequality and rigidity of the pupils, abnormal reflexes, ataxia, Romberg, signs of aortic disease, atrophy of the testicle, perforated nasal septum, or some other manifestation of late syphilis.

In this case there is no intimation of syphilis outside the central nervous system, but as the neurologic findings might be due to syphilis it is desirable to consider the bearing of the laboratory findings on this diagnosis. It is not uncommon to find the Wassermann test negative on the blood and positive on the spinal fluid in cerebrospinal syphilis. In this case both blood and spinal fluid are negative. Does this exclude syphilis? A negative Wassermann test cannot be regarded as a reliable exclusion of late cerebrospinal syphilis when the disease is inactive, and in certain cases of this type the Wassermann test becomes positive after antisyphilitic treatment. The negative test must be judged in connection with other features of the case and no absolute reliance placed on it alone. Here we have objective clinical evidence of an actively progressive disease with increase of protein in the spinal fluid and negative Wassermann tests, and such a combination is an almost certain exclusion

of syphilis. If it were thought desirable an attempt might be made to provoke a positive test by the intravenous use of salvarsan. We do not now use the luetin test.

The large number of diagnoses of syphilis in this case imply a lack of faith in the reliable exclusion of syphilis by clinical and laboratory means, and indicate a persistence of the feeling which prevailed before the laboratory diagnosis of syphilis had reached its present stage of development, that antisiphilitic treatment should first be tried and found wanting in all obscure cerebrospinal conditions before syphilis could be excluded.

The cell count on the spinal fluid showed 8 cells, which is slightly high, regarding 5 as the upper limit of normal. Lange's colloidal gold chlorid test has not proved satisfactory in our hands, and the contradictory evidence presented by it in this case illustrates how uncertain it may be.

The clinical picture is not inconsistent with tabes dorsalis in the clumsiness of the lower extremities, but stiffness is out of accord with involvement alone of the dorsal columns of the cord and implies a disturbance of the anterolateral tracts as well. Combined lesions of the dorsal and anterolateral tracts are observed in taboparesis, but we do not expect any such degree of sensory impairment in either tabes or taboparesis, and the dissociation of sensory perception serves to take the case out of this group entirely.

Ten physicians regarded the condition as a disturbance of the motor pathway as indicated by the diagnosis of spastic paraplegia or lateral sclerosis. The clinical aspects of the patient under discussion bear no close resemblance to any of the usual types of motor system disease commonly classed under progressive muscular atrophy. The onset in the feet rather than the hands, the absence of atrophy, and the presence of sensory impairment take the case out of this group.

The diagnosis of ataxic paraplegia was made by 7 physicians, 6 of whom, as already noted, recommended antisiphilitic treatment. In ataxic paraplegia there is spastic paraplegia and ataxia due to involvement of the lateral and dorsal columns. Inco-ordination is a prominent feature, but sensory impairment

is lacking and the sensory disturbances here make ataxic paraplegia an unlikely explanation of the symptoms.

Three physicians made the diagnosis of multiple sclerosis, but the absence of nystagmus, intention tremor and scanning speech, and the presence of marked sensory disturbances are against this diagnosis.

There is much to suggest syringomyelia, a diagnosis of which was made by 3 physicians, 2 of whom recommended antisyphilitic treatment. It is the only condition thus far discussed with which the given combination of sensory and motor impairment is almost wholly compatible. The dissociation of sensory perception with lack of impairment of touch and loss of pain and temperature sense, and the spastic condition in the legs are in accord with a degenerative process, such as a gliosis affecting the neighborhood of the central canal, the pathways for pain and temperature in the peri-ependymal gray matter and the pyramidal tracts. Muscular atrophy and trophic disturbances common to syringomyelia are lacking and the sharp limitations of the sensory impairment above at the level of the nipples and the angles of the scapula are against this diagnosis. Syringomyelia cannot, however, be excluded.

With these considerations out of the way let us analyze the evidence more closely to determine what justifiable conclusions can be drawn. It is clear from the clumsiness on walking, tendency to stumble and fall, difficulty in raising the feet, increasing stiffness of the legs, exaggerated deep leg reflexes and ankle- and patellar clonus, that there is involvement of the pyramidal tracts in the cord. The greater ankle-clonus on the right, the Babinski only on the right, and the greater weakness of the flexion and extension of the right leg suggest that the right side of the cord is more involved than the left. The diffuse or focal character of the lesion can hardly be determined from the motor symptoms. The slight increase in the deep reflexes of the arms suggests some motor involvement as high as the lower cervical region, and the inequality of the pupils, perhaps due to interference with the ciliospinal center in the lower cervical region, offers some confirmation of as high a level of cord dis-

turbance as this. But important evidence is presented by the evolution of the sensory impairment, and it is fortunate that it is possible to follow it through the earlier stages of dissociation of sensory perception. Evidently almost at the onset of the illness there was a loss of thermic and pain sense affecting the left leg more markedly than the right, while at this time tactile sense was everywhere unimpaired. As the illness proceeded, however, the disturbance progressed through a stage of dissociation of sensory perception to almost complete loss of all sensory impressions, to as far upward as the nipples in front and the angles of the scapulæ behind. These are most significant features, and indicate that the disturbance began as a unilateral or prevaillingly unilateral lesion of the cord. Owing to the conduction of the afferent paths in the opposite side of the cord in man the initial sensory disturbance in the left leg is to be ascribed to a lesion in the right side of the cord, thus confirming the suggestion from the motor manifestations of a right-sided lesion. The sharp limitation of the sensory impairment at the level of the nipples and angles of the scapulæ indicates a disturbance in the cord as high as the fourth or fifth thoracic segment.

What may be the nature of the disturbance? The slow progress and character of the symptoms suggest a compression myelitis of the cord. Of the various possibilities, aneurysm, fracture, and caries of the spine are unlikely from the negative x-ray examination. Syphilis may be excluded by the physical examination and special tests. Such parasites as echinococcus and cysticercus are unlikely in this part of the world. The echinococcus fixation test may be of assistance in excluding the former. Hemorrhage into the cord is usually of traumatic origin and there is no history of trauma. It is not to be entertained as an explanation here because of the progressive character of the symptoms. Hemorrhage is rapidly fatal or followed by complete or partial recovery, and persistence of some residual palsy.

A slowly growing tumor is the most likely explanation of the symptoms, but we cannot determine its nature. There is

no suggestion of a primary malignant growth to which a spinal tumor might be secondary, and a tumor primary in the cord or meninges may be the explanation. Such a tumor may be tuberculoma, sarcoma, fibroma, lipoma, psammoma, myxoma, neuroma, etc.

Can the differentiation be made between a medullary and a meningeal growth? As already noted, a gliomatous growth about the central canal of the cord cannot be excluded, though the clinical picture is not wholly consistent with syringomyelia. Extradural or intradural growths of meningeal origin commonly cause pain which is an early persistent and troublesome feature, while intramedullary tumors are likely to be painless in the early part of their course and until enlargement causes pressure on the sensory nerve roots. Pain is not a troublesome feature here, and the suggestion is, therefore, that if tumor is present it is intramedullary. Inasmuch, however, as extramedullary tumors are not infrequently painless no certain conclusions can be drawn. If an intramedullary growth is present is it diffuse and infiltrating or focal? Unfortunately, no evidence bearing on this question can be obtained. It is, of course, an important matter, however, from the point of view of possible relief by operation.

Five physicians made a diagnosis of spinal tumor and 2 of the 5 recommended operation. Regarding operation, it may be said that it offers the only prospect of relief from an illness the persistent progress of which seems to lead only to complete incapacity. In our lack of certainty as to the exact nature of the underlying pathology it can be proposed only as an exploratory laminectomy, with the hope, however, that some remediable lesion may be found.

Will the removal of spinous processes and laminæ for the purpose of the exploration weaken the spine and thus lead to disability? Not to any considerable degree.

Assuming the successful removal of a tumor, what chance is there that the patient will recover from the degenerative changes already present in the cord?

It would seem almost too much to expect that the patient

could completely recover from such severe injuries to the cord developing over the course of two years. The outlook depends somewhat on the stage of the disease at the time of operation. If removal is successfully accomplished during the period of Brown-Séquard complex while there is dissociation of sensory perception and spastic paralysis the result is naturally better than when a later stage of flaccid paralysis is reached.

The clinical diagnosis may be made as follows:

- (1) Tumor of the cord (medullary)?
- (2) Syringomyelia?

The patient accepted the chance of operative relief. Dr. W. J. Mixter removed the third, fourth, fifth, and sixth dorsal spines and the fourth, fifth, and sixth laminae. A tumor irregularly lobulated, 4 by 2 cm., was found at the level of the fifth dorsal vertebra, protruding posteriorly and lying transversely. It was free except at the point of exit of the fifth right dorsal root, the dural sheath in this region probably representing the site of origin of the tumor. The early manifestations of right-sided cord lesion are thus to be explained. When the attachment at the point of exit of the fifth nerve was cut the tumor was removed, with the escape of considerable spinal fluid. Examination by Dr. Wright showed it to be a fibrosarcoma. The subsequent course has been most successful. At the end of eight weeks the reflexes were still active, but Babinski and ankle-clonus had disappeared, while motion and sensation were practically normal. She has remained perfectly well, resumed her work as a laundress, and writes eight years after the operation: "I have worked ever since I left the hospital and have never yet even a backache. When I think of the condition I was in at the hospital I feel that I am now someone else." That no weakness of the spine has followed the removal of the laminae may be indicated not only by her capacity to work as a laundress, but from the fact that she has also taken up fancy dancing!

P. A., a laborer, thirty-nine, single, was admitted August 12, 1895. His father died of unknown cause, his mother was alive and well. He was unable to recall any previous illness. Three days before entrance he developed dyspnea, cough with scanty expectoration, and pain in the left side. The right leg was larger than the left. The venereal history was negative. The appetite was poor, the sleep disturbed. The pulse was regular, of good strength and volume. The right border of the heart was at the midscapular line.

Lungs: Left, dulness from apex to spine of scapula, below, flatness with bronchial breathing, increased voice sounds, and numerous fine crackling râles. Tactile fremitus was diminished. In the right back at base over an area the size of the palm of the hand there were some fine crackling râles. Flatness over left front with the vocal sounds and fremitus absent. Occasional fine crackling râles.

Liver: No increase. Spleen: No increase. Abdomen: Tympanitic, not tender. Extremities: Right calf $17\frac{1}{4}$ inches in circumference; left, 12 inches. Patellar and plantar reflexes normal.

August 14th: Aspiration in ninth interspace outside of angle of scapula. Fluid bloody in color, 21 ounces. No increase in respiration or discomfort after aspiration. Aspiration fluid; specific gravity 1017, albumin $\frac{1}{2}$ per cent.

August 18th: Pain in chest slight. Sleep very poor. Appetite fair. Bowels loose (two to three dejecta). Feels about the same.

August 22d: On 19th, needle insertion in left chest, axillary line, and 24 ounces of clear reddish fluid aspirated. Slept very little; appetite fair; bowels regular. Temperature 100° to 101° F.

August 26th: Dull just above angle of scapula. Flat below. Fremitus increased since entrance. Apex-beat 2 inches inside nipple line. Remained in bed, was comfortable, but slept poorly. Left back dull to angle of scapula, flat below, with slightly diminished fremitus at the extreme base. Medium moist râles heard throughout, more at base. Expiration at left apex prolonged and higher pitched than at right. No râles

heard at extreme apex. Left front very dull to first interspace, with marked bronchial breathing and an occasional moist râle and increased voice sounds. Below, flatness with diminished respiratory murmur, but no râles. Fremitus very faintly present above, absent below.

August 27th: General condition improved. Temperature lower. Resonance in back good to extreme base and out to posterior axillary line. Slept fairly well. Bowels now regular. Slight soreness across chest from previous vomiting. No pain in abdomen. Physical examination otherwise negative as at entrance. Breath sounds normal. In front at posterior axillary line there was flatness from bottom up as high as fourth rib and dulness above. In back flatness throughout. In upper axillary region faint breathing and râles. Below, diminished breathing. Under clavicle fine râles with marked diminution in breath sounds. Over whole left front almost absent breathing.

After aspiration there was no material change in the chest signs. Naturally, with the withdrawal of such a small amount of fluid, the signs would be little affected. Although the enlargement of the right calf was noted in the physical examination at entrance, it had not attracted the attention of my visiting physician, and it was not until the patient had been several days in the hospital that I examined the leg more carefully and discovered a painless tumor 3 to 4 inches below the head of the tibia. The tumor was hard and non-fluctuant and had a length of 7 inches. In my ignorance I had at first supposed that the enlargement of the leg was due to circulatory interference, but I had not explained how. My visiting physician very quickly told me that the tumor was probably the focus and the lung condition a metastasis, and in this opinion he was right. A specimen was removed from the tumor, and the pathologist reported that it showed only normal muscular tissue. Although the incision was made $1\frac{1}{2}$ inches deep, it apparently did not reach the tumor, and in a few days another specimen was taken. The examination by Dr. Councilman showed a spindle-cell sarcoma. On questioning the patient again he stated that he had noticed a gradual change in the right leg

for about a year. The patient was in the hospital forty-eight days, during which time he lost in weight and strength. The final diagnosis was: Sarcoma of leg with metastasis of lung. Thus I learned a lesson in history taking and physical examination which has been of value to me since.

Case II.—Woman fifty-eight years of age, a housekeeper by occupation, who entered the hospital in 1916 when fifty-four years old because of a tumor which she had noticed for eight months at the base of the left breast. There was intermittent and shooting pain which she considered to be due to rheumatism until she consulted a physician, who discovered the tumor and advised removal. Her past history was negative; the menopause had occurred at fifty. The family history was unimportant. The physical examination showed normal heart, lungs, and abdomen. There was a firm, painless, freely movable mass in the left breast with marked retraction of the nipple. A tentative diagnosis of carcinoma was made, operation advised, and performed. All the tissues of the chest wall were removed to the intercostal muscles with a complete dissection of the axilla. Six days after the operation there was elevation of pulse and temperature, and in the base of the right lung there was bronchovesicular breathing with dulness and increased tactile fremitus. In six days the lung had cleared and seventeen days after operation the patient was discharged in a satisfactory condition to the Out-patient Department. We might digress here to state that the lung signs without the active appearances of an acute pneumonia were probably due to a small pulmonary infarction often spoken of as a postoperative or ether-pneumonia. I have seen this condition many times in civil, hospital, and military practice. It begins like an acute pneumonia, but in twenty-four to thirty-six hours we have only the signs of pulmonary consolidation, the general aspect of the patient being normal. She continued in good health until March, 1920, when she entered the hospital again, complaining of cough and shortness of breath. Three weeks before she had "caught cold," and after using some cough mixture she improved, but noticed that there was dyspnea, and orthopnea which was slightly

relieved when lying on the left side. She was fairly well developed and nourished, but showed some loss of weight. There were no palpable glands or abnormal pulsations. The left lung was flat from the fourth rib to the base with absent tactile fremitus and breath sounds. The right lung was normal and the right border of the heart was 6 cm. from the midsternal line. The scar in the left chest was not inflamed. Three days later the right border of the heart was 8 cm. from midsternum. A needle inserted in the seventh interspace withdrew 2 liters of bloody fluid, and eight days later an additional liter was obtained. No growth was obtained from the fluid. After seven days she was again tapped, removing 1320 c.c. of bloody fluid. As much fluid was withdrawn as possible to see if radiographs would disclose a carcinomatous mass in the lung, but in this we were unsuccessful. After the second tapping the right border of the heart moved back to 4 cm. from midsternum, no fluid appeared to be accumulating, the patient looked and felt so well that she was anxious to return home.

She was re-admitted in a month complaining of pain and shortness of breath. The physical signs were the same as at the previous examination. As soon as 2 liters of hemorrhagic fluid were removed her symptoms were relieved. Twenty days later 2 liters more were aspirated and again in ten days $1\frac{1}{2}$ liters. During this visit pain in the left shoulder and axilla was a marked symptom, generally relieved by aspiration. If you could have seen the patient at that time you would not have suspected from her appearance the presence of malignant disease, as she was fairly well nourished and of good normal color.

She re-entered in July, 1920 in good general condition. On the 7th $1\frac{1}{2}$ liters of hemorrhagic fluid removed, on the 16th $1\frac{1}{2}$ liters of chocolate-colored fluid, and on the 20th $2\frac{1}{2}$ liters of dark red fluid. She was discharged on the 22d at her own request. After discharge she felt well for a week, when dyspnea, cough, and pain returned, so she was admitted on July 31st. During this visit a liter of chocolate-colored fluid was withdrawn. She was again in the hospital from September 3d to the 8th for aspiration. From then until December 2d,

when she entered again, she was fairly comfortable until a week before entrance, when her pain, dyspnea, and cough returned. At this time a small firm irregular mass about the size of a walnut was found at the left Ludwig angle. During this stay of twenty-



Fig. 200.—Case II. Showing scar of breast operation and secondary growth in ribs and sternum.

one days only 44 ounces of fluid were obtained. The patient entered the hospital for the last time on February 7, 1921. The mass steadily increased in size and the emaciation became more marked. About every two weeks 1 to 1½ liters of fluid

were withdrawn. The temperature was normal throughout, the pulse averaged 100, and the respiration 25. The red count was 4,210,000, the white count 8000, and the blood-pressure 100/70. After seven weeks the course had been gradually



Fig. 201.—Case II. Showing front view. Note emaciation of arm and neck.

downward, the pulse becoming more feeble, the reds 3,800,000, the cachexia and emaciation increasing. The patient died April 17, 1921, retaining consciousness until the end. A partial autopsy was obtained (Dr. B. C. Shackford). At the second left costochondral junction there was a hard nodule, the size

of a hen's egg, in the center of which was a small granulating ulcer about the size of a dime. The nodule was adherent to

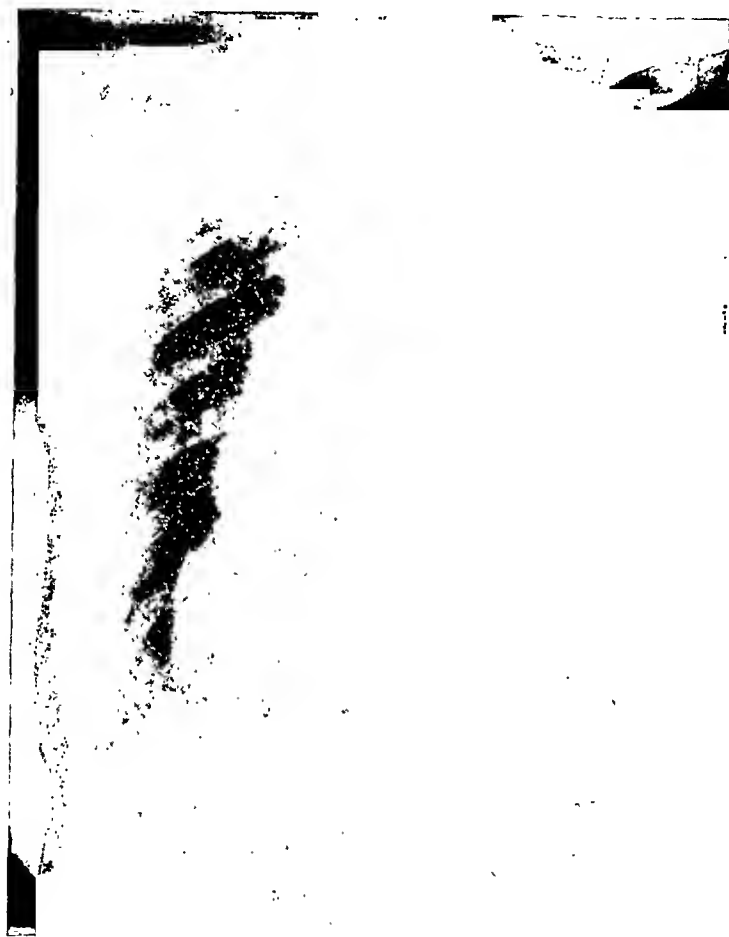


Fig. 202.—Case II. Dense shadow of left chest. Heart displaced to right. Fluid and greatly thickened pleura. Lung shrunk to one-fourth normal size. Very little change in picture after aspiration. Diagnosis made on history and fluid.

the underlying ribs and intercostal tissues which were thickened. Sections through the nodule revealed a finely granular, white

surface. Peritoneal cavity not remarkable. Pleural cavities: Right contained 500 c.c. of thin bloody fluid. Dense fibrous adhesions bound the lung to the diaphragm and united the two layers of the pleura along the root of the lung. Left contained about 800 c.c. of bloody fluid. The pleura was greatly thickened, shaggy, and adherent to the ribs in the region about the apex and about the nodule already described. The diaphragmatic pleura contained several firm white nodules, about 2 cm. in diameter; several smaller nodules were found scattered throughout the costal and visceral pleura; there they were obscured by the presence of fibrin and fibrous tags. Lungs: Right was negative except for a firm thickening of the pleura at the base, posteriorly. Left was collapsed about the tubes, each lobe was about the size of the fist, and held down by fibrous and fibrinous adhesions. Section showed a gray surface with thickened pleura. The lung did not crepitate. The pericardial cavity contained about 100 c.c. of thin blood-tinged fluid. The pericardium was thickened and nodular and adherent to the pleura, especially on the left. The gastro-intestinal tract was negative. The liver was not remarkable except for a firm, yellowish nodule, the size of a pea, near the diaphragmatic surface. There were no masses in the kidneys. The chief anatomic diagnosis was metastatic carcinoma of the left pleura, chest wall, pericardium, and liver, secondary to carcinoma of the left breast.

Case III.—Female sixty years old. Except for an occasional attack of bronchitis the patient has always been well and vigorous, but recently has been tired by the constant care of an invalid mother and her exertions in Red Cross work. Her family history was excellent. She was seen in December, 1919 in consultation with Dr. H. L. Houghton, to whom I am indebted for careful notes. About six months before she noticed a gradual loss of 20 pounds in weight and slight dyspnea on exertion. One month before there was breathlessness on climbing stairs. There had been some cough without temperature and her pulse, morning and afternoon, was 104° F. There were no hemorrhoids and no vaginal bleeding since the menopause, five years

before. There was no pain in joints or muscles. The appetite was poor, but digestion good. The bowels moved readily with the occasional assistance of a mild cathartic. On physical examination I found a cheerful looking woman, well developed and fairly well nourished, slightly cyanosed and dyspneic, sitting up in bed. The pulse was 104, of fairly good strength and volume. The throat and teeth were normal. There were no cervical, axillary, or inguinal glands. The breasts were

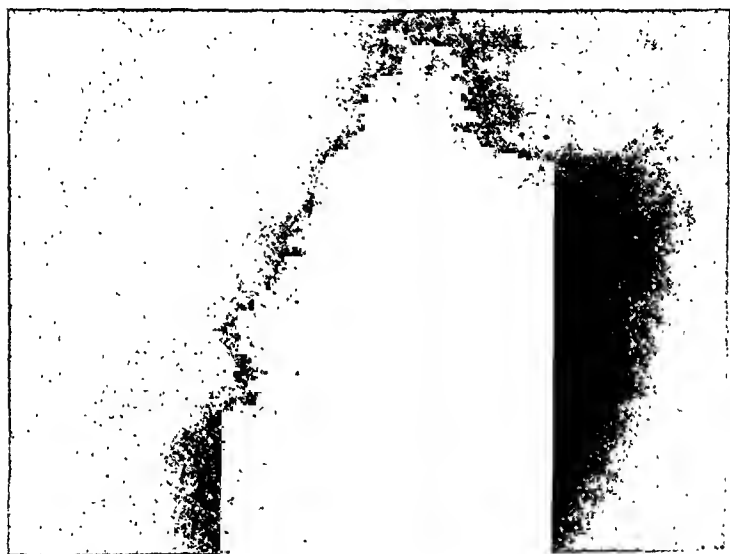


Fig. 203.—Case III. Shows the right chest filled nearly full with fluid, displacing heart to the left. There are several dense shadows just out from the hilus of the left lung.

normal without masses, retracted nipples, or discharge. The heart was normal in position and size with only a slight systolic murmur in the mitral area. There was extreme dulness above the spine of the right scapula with almost absent breath sounds and little change in the spoken voice. In front there was no change in physical signs except moderate dulness. At the right base there was flatness with absent breath, voice sounds, and tactile fremitus. Just before my first visit and again four

days after, Dr. Houghton removed $1\frac{1}{2}$ pints of serous fluid at each aspiration, thereby lessening the hoarseness, dyspnea, irritating cough, and dysphagia. Immediately after the second aspiration an x-ray plate was taken by Dr. L. B. Morrison. The lung was not tied down and no mass was seen. Dr. Morrison reported as follows: "Plates taken of the chest in the upright and supine positions. Some of the fluid has been withdrawn

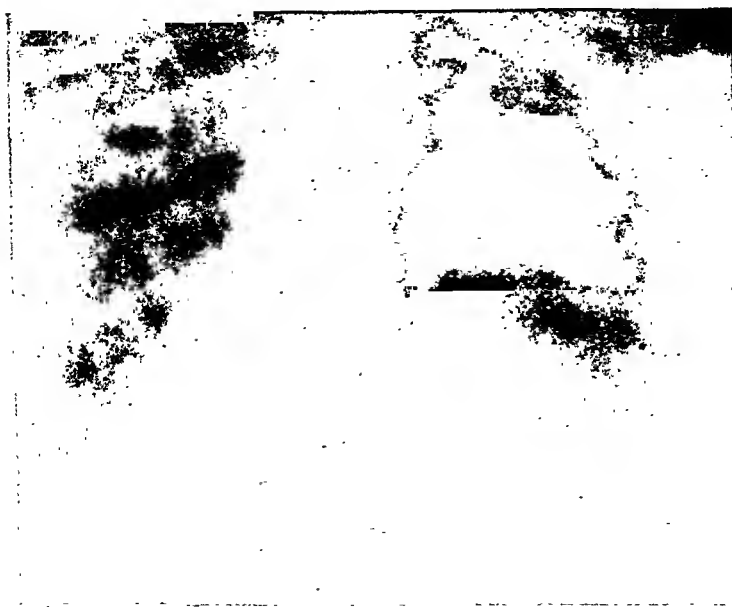


Fig. 204.—Case III. Taken a few days later following thoracentesis; shows still a small amount of fluid at the base of the right lung with pneumothorax and with an irregularly collapsed right lung. The heart shadow has changed its position somewhat. Plates were taken with a portable machine.

and there is now a hydropneumothorax. the lung is practically collapsed. its upper portion is opposite the fifth rib posteriorly, and extends out to the midclavicular line. On account of the collapsed state of the lung I am unable to determine any definite evidence in relation to the character of the lesion in the lung itself." Before the first aspiration Dr. Morrison made stereoscopic plates of the chest.

On January 10th I saw the patient again. During the previous three days the appetite was noticeably poorer and the general weakness greater. Her almost unproductive coughing attacks were preceded by sweating. At times small amounts of sputum were raised, but the examinations were negative for tubercle bacilli. She complained of a sense of fulness in the neck just above the clavicle, but no mass was palpable. There was hyperresonance from the right clavicle to the fourth space extending into the axilla; inspiration had a sonorous amphoric quality and the spoken voice a bell-like tone. The signs of pneumothorax were present, confirming the x-ray picture of a few days earlier. In the back over this area the note was dull, with little change in the distant voice and breath sounds. On forced inspiration air could then be heard down to the angle of the right scapula. At the base below the angle the note and other signs were those of pleural effusion. The pneumothorax if due to aspiration would not have persisted for two weeks, and would have been, as it generally is, at the site of exploration. It was, of course, caused by the breaking down of the neoplasm at the hilus. Three weeks later a specialist in tuberculosis saw her with us at this time, and agreed that it was malignant disease, probably carcinoma of the lung. The absence of tubercle bacilli after repeated examinations, the afebrile course, the radiographs, and the age of the patient were all against tuberculosis. He made what seemed to me an untenable premise in stating that had the patient been under forty-five, tuberculosis could have been less easily ruled out. To be sure, tuberculosis is a disease of the earlier decades, yet even those of us who do not deal exclusively with tuberculous patients see it often enough in the elderly to make it a substantial element in differential diagnosis. Two years ago a man of sixty-five years entered my service with diarrhea, emaciation, and weakness. Just within reach of the examining finger was a constricting ring in the rectum, which on examination by several competent surgeons was pronounced carcinoma. He had a few scattered crepitant râles, but the radiographs and slight sputum were negative. As he progressed to euthanasia

the ring became more dense and the opening smaller, but at autopsy he was found to have a tuberculous stricture.

Case III died two weeks after this last consultation without developing any new signs. Unfortunately, an autopsy was not obtained, but by elimination the diagnosis of primary malignant disease of the lung was made. Several examinations of the sputum failed to show the tubercle bacillus. The pleural fluid was examined three times. It was not hemorrhagic at first, as is often the case in malignant disease, but the second specimen was, and contained organisms due to the pneumothorax. The other specimens did not show a growth.

The laboratory examinations of the fluid were as follows:

Pleural Fluid.

December 19th:

Specific gravity.....	1.020
Albumin.....	1.26 per cent. by weight
Cultures.....	Negative
Endothelial cells.....	60 per cent.
Lymphocytes.....	29 per cent.
Eosinophils.....	1 per cent.
Neutrophils.....	Occasional
Blood disks present.	
No clot.	

December 30th:

Color.....	Red
Specific gravity.....	1.019
Albumin.....	1.1 per cent. by weight
Cultures.....	Bacilli
Sediment:	
Lymphocytes.....	40 per cent.
Endothelials.....	20 per cent.
Eosinophils	40 per cent.
Blood.....	Abundant

January 17th:

Specific gravity.....	1.020
Albumin.....	18 gm. per liter.
Cultures.....	Negative
Red blood disks.....	Numerous
Lymphocytes.....	65 per cent.
Eosinophils	17 per cent.
Endothelials.....	18 per cent.

The white count on two occasions by different examiners was 11,000, lymphocytes 17 per cent., and red cells 4,500,000. The urine showed only a slight interstitial nephritis. Every possible focus was investigated, as the nose, throat, tongue, breasts, digestive tract, uterus, kidneys, and rectum, without finding signs or symptoms. On physical examination over the area already described (just below the spine of the right scapula) there was a flat note and other signs similar to those of pleural effusion which persisted after aspiration. In addition to the flat note there was a boardlike resistance. This striking resistance with almost absent signs on auscultation have always seemed to me highly suggestive of neoplasm. I have been struck by its presence in every case I have seen.

The diagnosis was primary carcinoma of the lung.

Case IV.—A widow, age sixty-nine years, seen once in consultation with Dr. H. E. Faulkner, of Keene, N. H. The patient stated positively that she had always been well with the exception of whooping-cough one year before. The duration of her present illness at the time I saw her had been two months. She looked fairly well and said that she sometimes lost as much as 10 pounds in hot weather, but during July and August her loss had been only 3 pounds. She ate well, with a good appetite. Her sleep was undisturbed and her only discomforts were moderate dyspnea and pain in the left side. In view of the intense flatness of the left chest with the absence everywhere of breath and voice sounds it seemed probable that she had either tuberculosis or malignant disease with effusion. Because of several negative sputum examinations, normal temperature, and the patient's age, tuberculosis seemed less likely than malignancy. She died three weeks later and at the autopsy by Dr. O. H. Hubbard the left pleural cavity contained about 3 pints of fluid, the lung was small and firm, without crepitation. Large adhesions at the apex were so firm that the pleura was torn from the chest wall when an attempt was made to break them. Smaller and less firm adhesions were found between the lower lobe and the diaphragm. The lung tissue was pale gray except the lower lobe, which was mottled, red, and gray. A hard

firm mass, the size of an English walnut, at the root of the left lung surrounding the bronchus. On histologic examination the mass was found to be carcinoma. The right lung was emphysematous. No masses were found in any of the other organs. The anatomic diagnosis was primary carcinoma of the lung.

Case V.—J. B., a laborer, forty-seven years old, entered the hospital February 3, 1921, having been under the care of a competent surgeon, who was in doubt about the diagnosis, but thought the patient probably had a gastric carcinoma and sent him to the hospital for a bismuth series. His family history was negative; there had never been any tuberculosis or cancer, and the patient had not been exposed to tuberculosis by immediate contact. He claimed that he had never known an hour of illness until the beginning of the present sickness last October. He began with pain in the lumbar region and nocturia, but at entrance the latter only persisted. He had a sense of fulness and distress in the epigastrium immediately after meals, with eructations and intense nausea, but without vomiting. His appetite was good, he enjoyed food, but ate very little because of the distressing symptoms. At this time he developed a cough which had persisted, with large quantities of thin white sputum. The temperature before entrance and during his residence in the hospital was always normal. With his progressive emaciation, cough, and weakness he had never had night-sweats. The pulse had ranged between 90 and 110. The examination disclosed a well-developed emaciated man, slightly cyanotic and dyspneic. The loss of weight was striking. The general examination was largely negative as to throat, mouth, teeth, tongue, glands, or pulsations. The heart was not remarkable. The resonance throughout the lungs was generally poor, and in the base there was flatness, with boardlike resistance and absent auscultatory sounds. A radiograph taken two days after entrance showed consolidation of the right and left bases with thickened interlobular septum on the right. There was a little fluid in both bases. Two bismuth series were done, with negative results. The liver was not enlarged and there were

no abdominal masses. The bowels could be moved readily with cathartics. The rectal examination was negative; prostate



Fig. 205.—Case V. Plate taken about two and a half months before death. Fluid at both bases. Both lungs infiltrated with tumors from size of a pea to a hen's egg.

not enlarged. The bones and muscles were negative. I was not sure of the diagnosis in this case, but I would like to discuss

the differential points. My house physician felt that it was fibroid phthisis, but the patient was perfectly well until five months ago. I know this not only from his statement, but his physician's, who had known him for ten years. He was well, without cough or dyspnea, and able to perform laborious work. The patient died two months after leaving the hospital, and an autopsy was performed on April 26th by Dr. King, of the Boston City Hospital. Both pleural cavities contained about a liter of bloody fluid. The lungs were infiltrated with many firm gray nodules varying in size from a pea to a hen's egg. The peritoneal cavity contained about 2 liters of bloody fluid, with several masses on the mesentery similar to those in the lungs. The right kidney was irregularly enlarged to about four times the normal and contained several firm masses. There was a firm tumor about the head of the pancreas.

Anatomic diagnosis: Carcinoma of the kidney with metastatic carcinoma of the lungs.

The kidney had not been felt while the patient was in the hospital, and the negative examination of all other possible sites might have given this case a clinical classification of primary carcinoma of the lung.

Symptomatology.—The onset is very gradual and the general appearance may not in any way suggest the seriousness of the condition. Cases II, III, and IV did not appear ill; the color and nutrition were good. Case II was under our care for eight months before the cachexia of malignancy began to appear. Case III lost very little in weight, and aside from a moderate cyanosis maintained a fairly healthy appearance almost to the end. Case IV came to my office from another state, and seemed in fairly good general condition, although she died about a month later. The pressure symptoms vary greatly, dependent on the position, size, and rapidity of growth. Tumors within the lung cause less pressure symptoms than those at the hilus, and those of the latter site much less and more slowly than growths of the mediastinum. In our cases the local symptoms were dyspnea, cough, distress from pressure, and pain.

Dyspnea.—This symptom is the first, most constant, and

most progressive. It is the one which brings the patient to the physician. The dyspnea was lessened very materially in 3 of our cases by aspiration, and while never entirely absent, it gradually returned with the fluid. Orthopnea was absent to the end in 3 cases. Cough and pain: Cough was present in every case, but it varied greatly. Pain was an infrequent symptom. Case II was almost free from cough during her entire illness, yet at autopsy the pleura was tremendously thickened, firmly adherent to the chest wall and the diaphragm, and the left lung gray and compressed to the size of a man's fist. Notwithstanding the marked pleural involvement pain was generally absent. Whenever she complained of pain, never severe or enough to prevent sleep, it was relieved by aspiration, after which she would be comfortable until two or three days before the next tap.

Case IV had much the same pleural involvement, coughed moderately, but had considerable pain. Case III, with a growth at the hilus, had a dry, "brassy," irritating cough with very slight sputum. Pain was very moderate and relieved by aspiration. Case V had considerable cough, especially in the morning, raising moderate amounts of thin mucoid sputum. Case I had dyspnea, cough, scanty sputum, and pain in the left side, but as soon as the pleural fluid was removed the pain and cough became inconsiderable factors.

General symptoms: Although one would expect the same early general weakness, emaciation, and cachexia of other sites of malignancy it is remarkable how long these symptoms may be delayed. Four of our cases maintained an appearance of reasonably good health almost to the end. The fifth case had marked progressive weakness and emaciation from the beginning of his local symptoms. The pallor and loss of weight in my experience have never been so great as in malignant disease of the stomach because food is well borne for some time after the local symptoms have declared themselves. Of course, there are the cases where constitutional symptoms antedate the local, particularly in deep-seated primary growths.

Diagnosis.—In secondary cases with a known focus of

malignancy the diagnosis is fairly simple *if one has the possibility of metastasis in mind*. If a focus outside of the lung cannot be found the diagnosis naturally is as difficult as in primary malignant disease of the lung. Involvement of the mediastinum generally gives earlier and more striking local signs due to interference with the circulation, as in lymphoblastoma and less frequently in aneurysm. After aspiration the x-ray may show the tumor, but it is not always helpful, especially with small primary growths. After aspiration, *the persistence of an area of extreme dullness, with diminished tactile fremitus and nearly absent breath sounds above the area where the fluid was*, has been a helpful sign to me. If the fluid is hemorrhagic it is very suggestive of malignancy. If there is persistent pleurisy, generally with constantly recurring fluid, especially in an elderly person, it usually means malignancy. A search for particles of the tumor in the pleural exudate or sputum has never rendered satisfactory results in our hands. If tuberculosis is present, thorough and repeated examinations of sputum will usually disclose the tubercle bacillus. In our cases the temperature has been practically normal throughout. The white count has always been higher than is usual in tuberculosis, an average of 2,000.

Cirrhosis of the lung is essentially chronic and extends over a period of years. There was no history of a predisposing pulmonary origin. The condition is generally unilateral, and in a patient as ill as J. B. tubercle bacilli would usually appear in the lung, but none have been found after repeated examinations. The amount of sputum was much smaller than I have usually seen in fibroid phthisis. In addition, the heart was not enlarged as it always is in this condition.

Syphilis of the lung is very rare. Osler found only 12 cases in 2800 postmortems at the Johns Hopkins Hospital, and in 8 of these cases the lesions were in congenital syphilis. There was no evidence of syphilis elsewhere and the Wassermann reaction was negative. Mallory does not mention it in his book, and Delafield and Prudden refer to it, speaking briefly of the cases of congenital syphilis.

Cases of primary carcinoma of the lungs are so uncommon that without postmortem confirmation the diagnosis is offered with considerable trepidation. This disease is generally secondary to some focus which may or may not be discovered during life, but Adler collected 374 cases of primary carcinoma and 90 of primary sarcoma of the lung. Sailer and Torrey gathered statistics showing 130 primary carcinomata of the lung in 87,451 autopsies. Sarcoma of the lung is much less common; Passler found among 1000 cases of malignant disease 16 cases of primary carcinoma and 4 of primary sarcoma. At the Boston City Hospital in 27,135 medical patients there were 14 cases of primary carcinoma and 2 with sarcoma; 10 with secondary carcinoma and 2 with sarcoma. In the secondary carcinomata the locus was 5 breast, and 1 each from uterus, kidney, pylorus, intestine, and ovary. In secondary sarcoma 1 from intestine and 1 from kidney.

When I was house physician in this hospital I showed my visiting physician what I considered a primary carcinoma of the liver, but he informed me that I was mistaken, that primary carcinoma was very rare and an undiscovered focus existed. At the autopsy he proved to be right, as there was a very small primary growth near the pylorus. Since then carcinoma of the liver has been found more frequent and so it may be with the lung. Karsner found in the records of 2000 autopsies in the Lakeside Hospital only 3 cases of primary cancer of the lung, and none in 1000 autopsies in the Cleveland City Hospital. Both of these are general hospitals and have very little material from wards for tuberculous patients. Karsner believes the incidence given in these figures to be extremely low, and from the studies of Ash at the Boston Tuberculosis Hospital is inclined to think the number would be larger if the two Cleveland hospitals had any wealth of tuberculous material. In addition to the 3 cases mentioned he has recently had one of primary carcinoma in a private autopsy. Karsner discusses the viewpoint of the pathologist in these cases, stating that importance attaches to the question as to whether tumors originate solely in the bronchi or may originate from the alveoli. The power of regeneration

after injury is certainly greater in the bronchi than in the alveoli. This would be expected from the fact that bronchial epithelium represents a lesser degree of anatomic differentiation from the primary gut tract than is true of alveoli epithelium. It is well known that most of the cells in the alveolar surface are not nucleated, and there is some question as to whether or not there are nucleated cells in this position. It has been claimed that regeneration of alveolar epithelium occurs, but it has not been proved with entire satisfaction that the cells are not extensions from regenerating bronchioles. Power of regeneration signifies power of proliferation under the influence of unknown stimuli, which stimuli may be similar to those which lead to malignant proliferation. It would therefore seem reasonable to expect that most primary cancers of the lung originate in the bronchial epithelium.

A report has recently been made of carcinoma of the lung following closely attacks of epidemic influenza. In one of our cases primary carcinoma followed one year after whooping-cough and in another after repeated attacks of bronchitis.

Tuberculosis is the most common condition which the physician confuses with malignant disease of the lungs. Funk states that among 1200 patients sent into the wards of the Chest Department of the Jefferson Hospital with a diagnosis of advanced tuberculosis, 72 were incorrectly diagnosed, and of that number 5 had malignant disease of the lung.

In 1906 Jessen wrote on the combination of pulmonary carcinoma with tuberculosis, and stated that it was rarely diagnosed during life. He regarded it as a rare condition in which the finding of tubercle bacilli masked the true picture. Norris and Landis state that among 662 autopsies at the Phipps Institute there has been no instance in which the two diseases occurred together. Ross in a study of 60 cases of malignant disease found tubercle bacilli in 2 patients. Wolf believes the combination to be fairly common, having tubercle bacilli in 23 out of 31 cases of malignant disease. There are wide differences of opinion on this question throughout the literature.

In our cases repeated examinations of the sputum were made.

Treatment.—We naturally think of operation, especially in primary malignant tumors, but it must, as in all malignant growths, be performed early, and the difficulties of prompt diagnosis have already been considered. Seydel studied the question on autopsy material, and concluded that 26.9 per cent. of lung sarcomata are operable and a little larger percentage of pleural sarcomata. Carcinoma showed 9 per cent. as favorable. The treatment so far has been symptomatic. Thoracentesis has been repeated as often as the physical examination has indicated the return of fluid or when the patient is again distressed by pain, cough, and increased dyspnea. The procedure has always been followed by varying periods of comfort; sometimes, as in Case II, of considerable duration. Kuttner has done palliative operations in carcinoma, but no results of value have been obtained. We all look to the x-ray with hope that the brilliant effects produced on lymphoblastomata may be repeated in cases with carcinoma, but we fear that it is only lymphoid tissue which yields. One of our cases was rayed without results, but it is only fair to state that the condition was very advanced before the treatment was used. Osgood, of the x-Ray Department, makes the following statement concerning the treatment of these cases: Recent developments in the treatment of malignant disease, clinical and experimental, seem to show that the success of the x-ray treatment of these conditions depends primarily on the administration of a lethal dose to the site of the lesion; and, furthermore, that the dose should be delivered *en masse* and not in fractions.

Sublethal doses may produce an inhibition which may persist for some time, but the later result is a compensatory increase in activity which may cause the tumor to develop much more rapidly than would originally have been the case. Prolonged radiation over a period of time may also produce in the tissues a certain amount of immunity to the rays. Thus it is that lesions apparently clinically cured may suddenly and quite unexpectedly develop a metastasis which spreads like wild-fire and upon which further radiation has apparently no effect.

While the resistance of cancer tissue is only about 65 per



Fig. 206.—A case of lymphoblastoma showing glands of thorax at the time of admission. Diagnosis made from tonsil by Dr. F. B. Mallory. Service of Dr. E. N. Libby, Boston City Hospital.

cent. of the adjacent normal tissue, the overlying skin has only a relative resistance of about 25 per cent. This, therefore, places a limit on the amount of radiation which can be delivered

to a lesion through any given area of skin. Clinically the maximum dose is that which will produce a moderate erythema



Fig. 207.—Lymphoblastoma. Showing improvement after four areas had been rayed by Dr. H. A. Osgood.

of the skin which appears in the average case about ten to fourteen days following the radiation, and may persist as a tan from one to six weeks thereafter.

This obstacle to intensive radiation can be met in two ways.

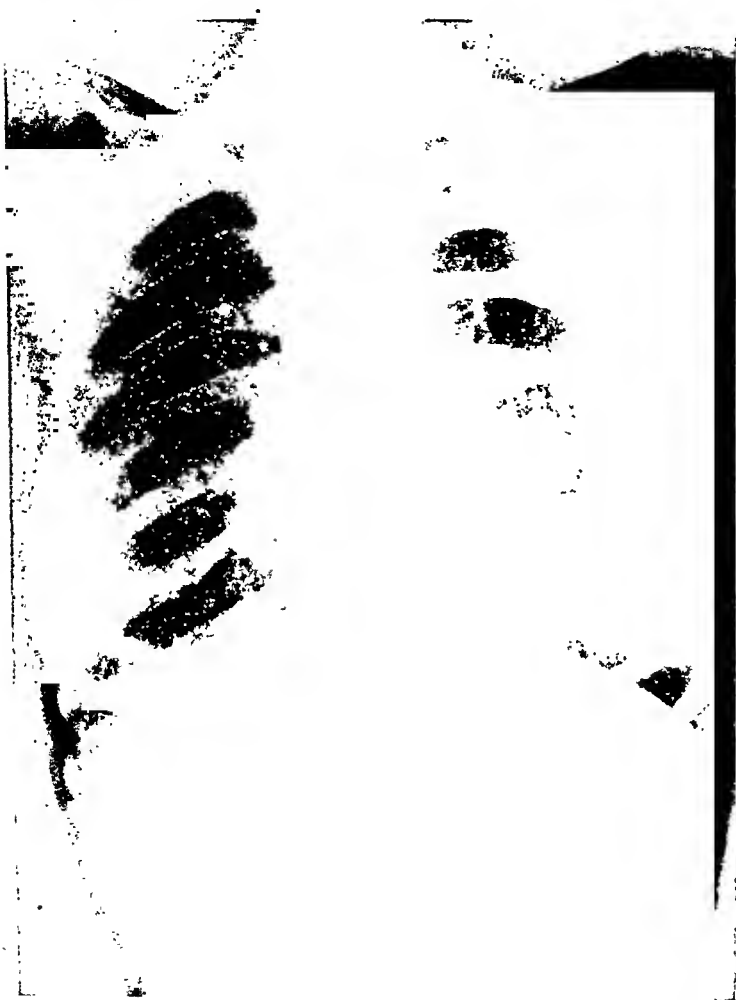


Fig. 208.—Lymphoblastoma. Plate taken at time of discharge of patient from hospital. Patient to report to x-Ray Department every two weeks for observation.

The first is the selection of several ports of entry through different areas of skin so chosen that the rays will cross-fire the site of the

lesion. Thus a deep-seated lesion can be exposed by raying from the front, the side, and the back of the body.

The second method is based on the fact that the efficiency of the radiation delivered to a given surface varies inversely with the square of the distance from the target of the α -ray tube to area to be exposed. Hence it is obvious that if the distance from the target to the skin were half that of the target to the lesion, then the skin would receive approximately four times the dosage as the lesion. If the distance is increased to the point where the difference between the distance to the lesion and the distance to the skin is comparatively small, then it will be possible to deliver to the lesion essentially the same dose as the maximum received by the skin. This means that the time of exposure must be correspondingly increased to compensate for the rays absorbed by the greater distance.

Another but less important limitation to the dosage is the toxic reaction which may follow the breaking down of the tissue. In lymphoid tissues this reaction may be quite marked, but in cancer it is relatively unimportant. The toxic reaction usually appears in from three days to a week after the exposure.

A third consideration is the so-called α -ray sickness. This is not due to the breaking down of the malignant tissue; it is thought to be due to changes which the rays produce in the blood; it is characterized by nausea, vomiting, and weakness, and may be so severe as to necessitate temporarily discontinuing treatment.

Clinical results in α -ray therapy indicate that the more penetrating rays of shorter wave length give better results in the treatment of deep-seated malignancy. The penetration depends on the voltage delivered to the α -ray tube. With our present equipment the maximum working voltage is about 70,000 to 80,000, although experimental equipment is being designed to deliver upward of 100,000 volts. The radiation actually delivered is not uniform, but includes all variations up to the maximum. These softer rays may produce a marked reaction in the superficial tissues without delivering sufficient penetrating radiation to influence the deeper tissues. This difficulty

is overcome by the use of copper or aluminum filters of varying thicknesses which shut off the less penetrating rays. The volume of radiation which emerges from the filters is correspondingly reduced. Therefore a longer exposure time is required to deliver the necessary dose.

In summary, modern x-ray treatment consists in the use of heavily filtered radiation at a relatively greater distance and a correspondingly increased exposure time. It is obvious that the expense of these treatments is much increased both on account of the time required and because of the greater strain to which the equipment is subjected. It seems possible, however, to secure results which have been hitherto unobtainable. The outlook for the future with improved equipment and technic is very promising.

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CLINIC OF DRS. PAUL D. WHITE AND
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THE CLINICAL SIGNIFICANCE OF CHANGES IN THE
FORM OF THE ELECTROCARDIOGRAM¹

As electrocardiographic records accumulate it becomes possible to study the variation in the curves of given individuals over a series of years, and to attempt to correlate the changes in the curves with clinical changes in the patients. The purpose of this paper is to record certain cases of changing ventricular complexes which we have observed over periods of years.

One of the most striking characteristics of the electrocardiogram is its constancy for a given individual. The individual curve, indeed, is so nearly of a fixed type that it has been suggested that the electrocardiogram be used as a means of identification. Now the configuration of the curve is determined by the path and the velocity of the excitation wave through the heart and the relation of this path to the lines of the three leads. The path of the wave is determined by the architecture of the conduction system; the rate of conduction by the functional ability of these specialized tissues. The course of the wave can be influenced by the conducting power of the specialized tissues at the moment because the wave will travel by the quickest route. The constancy of form of the electrocardiogram, then, is dependent upon the functional integrity of the conducting system. Variation in the curve implies a variation in the course of the excitation wave, hence a functional

¹ From the Cardiac Clinic of the Massachusetts General Hospital. Read in part before the Harvard Medical Society, Peter Bent Brigham Hospital, March 15, 1921.

change in the conducting tissues. Whether this change is permanent or temporary, whether the functional change is accompanied by discernible anatomic change or not, does not concern this general rule, which postulates merely that the configuration of the ventricular complex depends upon the course of the excitation wave through the ventricles, and that this in turn depends upon the distribution and functional ability of the conducting tissues.

The experiments of Rothberger and Winterberg¹ and of Lewis² suffice to illustrate the profound disturbance of conduction and the consequent deformity of the curve due to interference with the functioning of a main branch of the auriculoventricular bundle. Carter³ has summarized the clinical observations on 22 cases of bundle branch block. Oppenheimer and Rothschild⁴ have described changes in the electrocardiogram associated with myocardial changes particularly involving the subendocardial region. Recently the same investigators⁵ have succeeded in producing variations in the electrocardiographic curve by cauterizing the endocardial surface of the dog's ventricles. Subsequent examination of the injured hearts revealed damage to the Purkinje network. Robinson^{6, 7} has emphasized the importance of "functional fatigue" in cases of transient deformity of the initial ventricular complex. Wedd⁸ has followed a case for twenty-one months, taking consecutive tracings and observing progressive change. Willius⁹ analyzed 747 cases, and concluded that notching and slurring even in Lead III made the prognosis less favorable, an extreme view.

The following 5 cases, 4 of them under observation for periods of years, illustrate certain types of variation in the form of the ventricular complex:

Case I.—M. D. West Medical 212,632. **Cardiosclerosis. Auricular Fibrillation. Heart Failure.**—This patient, a white male, working as a watchman, entered the hospital in June, 1916. He was sixty-five years old.

His early history throws no light on his cardiac condition. He had not had rheumatic fever, tonsillitis, or chorea. He denied having had syphilis. Thirty-one years before this entry

(1885) he was treated in the hospital for injuries. No record was made of any cardiac abnormality.

In 1912 he entered the hospital with auricular fibrillation and clear signs of cardiac failure. Under rest and digitalis he improved rapidly, and in ten days was discharged, much improved. His diagnosis was recorded as arteriosclerosis, myocardial insufficiency, auricular fibrillation, chronic nephritis.

For a year after leaving the hospital in 1912 he felt very well; since then he had gradually gone down hill, but had continued at his work as a watchman until the day of his admission (1916). For a year he had had a hacking cough, which was worse during the winter. For two months he had been increasingly short of breath; for three weeks he had had to stop and rest on his way up stairs. For months he had observed occasional swelling of his legs; for three weeks it had been constant and progressive. Simultaneously his abdomen had increased in size. He had taken no digitalis.

Upon physical examination (June, 1916) he was found to be cyanotic and dyspneic in bed. His skin showed many keratoses. There was a slight general glandular enlargement. His pupils were unequal, irregular, and reacted sluggishly to both light and accommodation. His lungs were emphysematous and coarse moist râles were heard over both chests. Both lung bases were dull and the breath sounds were diminished over the dull areas. The apex of his heart was felt in the fifth intercostal space, 11 cm. to the left of the midsternal line. By percussion the heart lay 4 cm. to the right and 12 cm. to the left. The supracardiac dulness measured 7 cm. The heart sounds were absolutely irregular and of poor quality. The pulmonic second sound was greater than the aortic second sound. A systolic murmur was heard at the apex. No diastolic murmur was heard. The brachial arteries were tortuous. Taking the maximal beats the blood-pressure was found to be 180/100. There was marked edema of feet and legs. Reflexes were normal. Eye-grounds were negative.

His urine exhibited the slightest possible trace of albumin, and many hyaline and granular casts. Phenolsulphonephthalein

excretion was 20 per cent. in two hours. A Wassermann test on the blood was negative.

Report of electrocardiogram June 14, 1916 (Fig. 209): Rate 85; auricular fibrillation; ectopic beats; marked variation in shape of initial ventricular complex from beat to beat. This variation is not a mere waxing and waning with respiration, but an abrupt and considerable change. It is not a digitalis effect. A few beats are probably of ectopic origin.

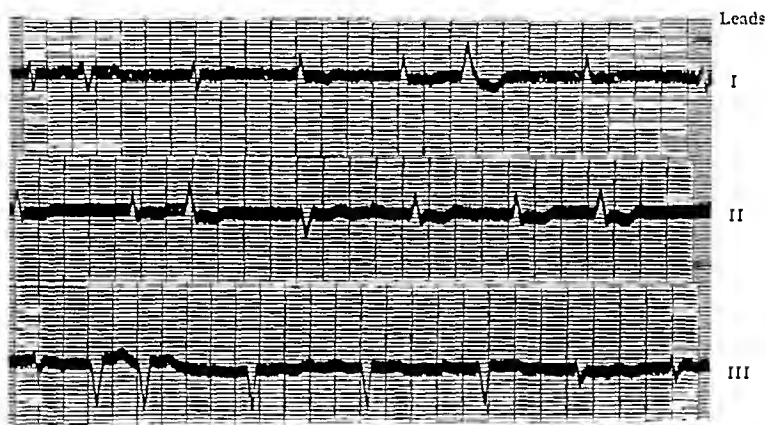


Fig. 209.—Case I. June 14, 1916. Auricular fibrillation. Marked variation in shape of successive QRS complexes. Probably ectopic beat in Lead I. Second and third beats in Lead III may also be ectopic.

(Leads I, II, and III in sequence in this and all succeeding figures. Ordinates = 10^{-4} volt in this and all succeeding figures. Abscissæ = 0.2 second in this and all succeeding figures.)

He responded well to treatment (*Digitalis folia*, 0.1 gm. t. i. d.), but only temporarily. Six months later he died. During the period of his relative comfort his tracing was less bizarre.

Discussion of Case I.—Cases of variation in the form of the QRS complex from beat to beat have been recorded by Cohn,¹⁰ Oppenheimer and Williams,¹¹ Christian,¹² and Robinson.^{6, 7} Many of the cases have been associated with auriculo-ventricular heart-block, partial or complete. In cases which vary from beat to beat we have obviously to assume that variation in the conducting power of the special tissues is taking place

almost continuously, with corresponding variation in the path of the excitation wave. Such variation has been ascribed usually to the cardiac malnutrition of severe decompensation, to digitalis intoxication, or to functional fatigue in hearts beating rapidly.

Illustrations of other types of transient variation in the form of the electrocardiogram are not hard to find. White and Stevens¹³ have described a remarkable curve showing the onset of typical bundle branch block during an attack of auricular flutter in which the ventricle was responding to every auricular impulse (273 per minute). With resumption of normal rhythm a few minutes later the curve returned promptly to a normal outline. A similar curve has been described by Lewis.¹⁴ The element of fatigue which has been emphasized by Robinson is illustrated by certain cases of aberrant ventricular complexes following auricular premature beats. White¹³ and Robinson⁶ have shown that the greater the prematurity, *i. e.*, the shorter the preceding period of rest for the conduction system, the greater the aberration. Finally, the variation in the P-R interval in cases of partial heart-block is an illustration of varying rate of conduction. A dropped beat with its associated rest period is followed by a shortened P-R interval.

In the case here described it seems probable that the impulse traveled through injured tissues which were easily exhausted, so that the routes traversed in successive beats were seldom exactly the same. The ventricular complexes became more normal coincidently with the patient's improvement under the administration of digitalis.

Case II.—J. B. Out-patient Department, 263,144. Cardio-sclerosis. Auricular Fibrillation.—This patient is seventy-three years old, a farmer. He has always been well except that thirteen years ago he had acute rheumatic fever associated with tonsillitis; at that time he was in bed for three weeks.

About seven years ago, when he was sixty-six years old, he began to be a little short of breath. Six years ago he came to the Out-patient Department complaining of dyspnea, edema

of the ankles, and slight precordial pain related to overexertion or overeating. Physical examination at that time revealed a white-haired old man without arcus senilis. He weighed 191 pounds. His radial arteries were readily palpable. The apex-beat was diffuse and forceful and easily felt in the fifth intercostal space 14 cm. to the left of the midsternal line. Percussion showed the right border of dulness 5.5 cm. to the right. A systolic murmur heard best at the apex was transmitted to the

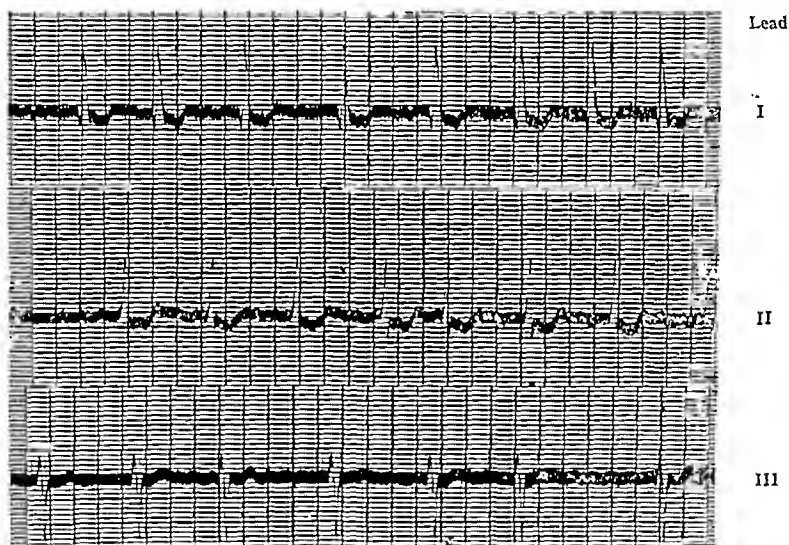


Fig. 210.—Case II. March 18, 1915. Paroxysmal auricular fibrillation. Strongly inverted T-wave (digitalis effect). QRS complex normal in outline.

axilla. A basal systolic murmur was transmitted into the neck vessels. No diastolic murmur was heard. There was no thrill. His pulse was 80 and quite regular. The heart sounds were of good quality. There was moderate edema of the ankles. Systolic blood-pressure was 170 mm. Hg. A urine examination failed to show albumin or casts. Wassermann on the blood was negative.

He was given vigorous digitalis treatment for two weeks,

at the expiration of which time he came in complaining of nausea. His cardiac symptoms were not relieved. His pulse was irregular in rate and strength, but there was no pulse deficit. His first electrocardiogram at this time (Fig. 210) showed auricular fibrillation, left ventricular preponderance, and an inverted T wave in Lead II. The initial ventricular deflections were of normal outline. The inverted T wave was presumably due to digitalis.

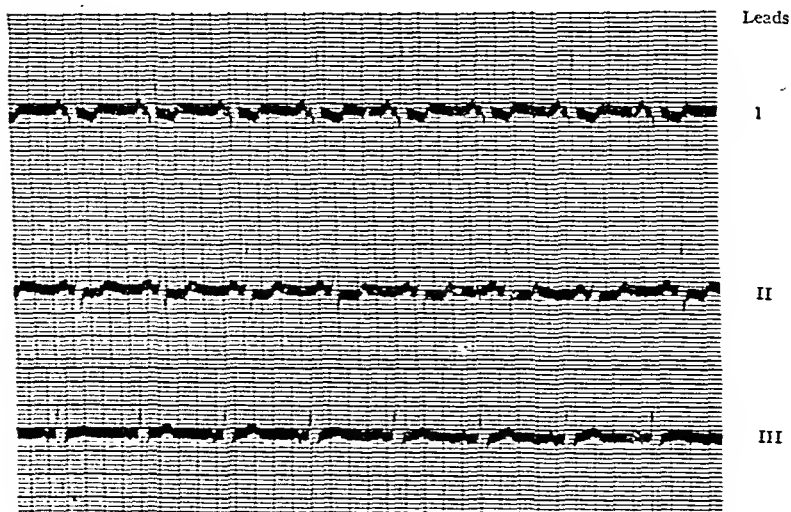


Fig. 211.—Case II. March 25, 1915. Normal rhythm. QRS complex as before. Inversion of T-wave less marked.

A Roentgen examination (7-foot plate) at this time was interpreted as follows: "Apex is in the fifth interspace 10.2 cm. to left of median line. Right border is 6 cm. to right of median line. Total transverse diameter 16.2 cm. Greatest transverse diameter of great vessels 5.6 cm. Length of heart 17 cm. Diameter at base 11.8 cm. Enlargement of both sides of heart."

The auricular fibrillation was felt to be paroxysmal in nature and due to excess of digitalis, so the drug was stopped. A week later he appeared with normal rhythm, a pulse of 78, and marked subjective improvement. An electrocardiogram at this

time showed a normal mechanism and the same QRS complex (Fig. 211).

He was kept on constant small doses of digitalis leaf and did very well, able to work cautiously about his farm most of the time. A year later he came complaining of more frequent and more intense precordial pain, only slightly relieved by

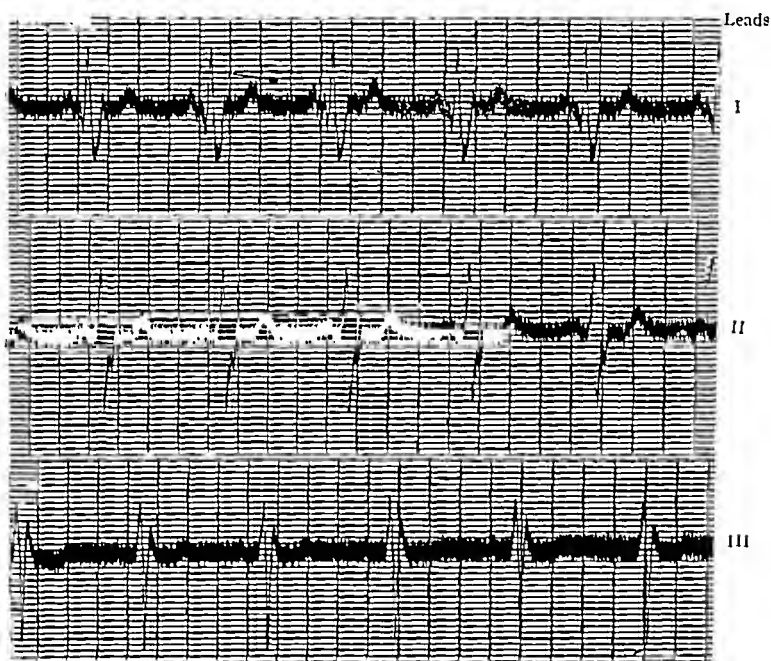


Fig. 212.—Case II. February 15, 1916. Normal rhythm. Great change in QRS complex, which exceeds 0.1 second in duration, has deep notches, and new slurrings.

nitrites. His blood-pressure was 150/90, his pulse-rate 84. His electrocardiogram at this time (Fig. 212) showed profound change in the QRS complex, which had become pathologically wide, with new slurrings, and in Lead II, where notching is of most significance, it was deeply notched.

Another year and his electrocardiogram (Fig. 213) showed notchings a little deeper. Some slurrings of last year were now

definite notches. His clinical condition was little changed, although he required more digitalis to keep him going comfortably.

On October 11, 1920 the following note was made on his record card: "Well all summer except for ache in left back when he gets tired or is exposed to a draft. It comes every few days and lasts several hours. No difficulty with micturition. No hematuria. No cough or headache. Bowels normal. No recent loss of weight. No pain in arms. Left leg occasionally swells. Heart has behaved quite well. He has taken 3 gr. (0.2

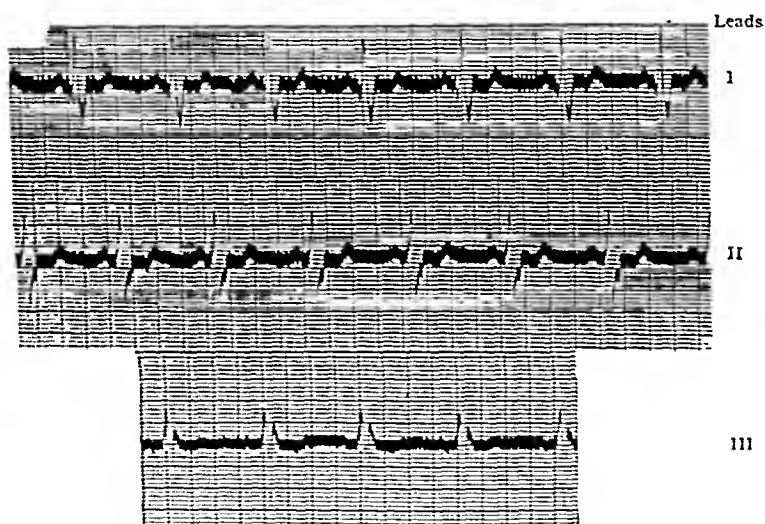


Fig. 213.—Case II. March 3, 1917. Normal rhythm. Notching a little deeper and complexes of lesser amplitude.

gm.) of digitalis leaf daily since May. Physical examination showed the apex impulse diffuse in the fifth and sixth spaces just outside the nipple line, 11 cm. to left of midsternum. Blowing systolic murmurs at both apex and base, rougher at the base. No diastolic murmur.

Pulse-rate:		
Apex...	108
Radial..	103
Deficit	5

His lungs were clear, the respiratory expansion normal. There was no costovertebral tenderness. Spleen and kidneys not felt. Slight edema over shins, especially on the left." His electrocardiogram (Fig. 214) showed auricular fibrillation, now permanent, and further variation in the form of the QRS complex. The amplitudes of the deflections were in the main reduced, which tends to mask somewhat the notches previously observed, which were still there. A new notch had appeared on the upstroke of the S wave in Lead III.

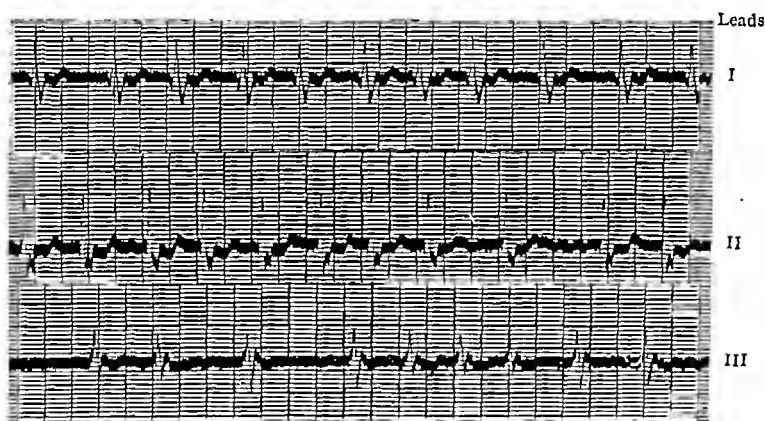


Fig. 214.—Case II. October 11, 1920. Auricular fibrillation (permanent). New variation in form of QRS complex.

He was last seen on April 1, 1921. He was feeling only fairly well, as he was taking digitalis of an unknown and evidently insufficient strength, and his heart rate had gone up.

Pulse-rate:

Apex.....	104
Radial.....	82
Deficit.....	22

His radial arteries were tortuous and beaded. The heart's apex was felt in the sixth space, 12 cm. to the left of the mid-sternal line. A blowing systolic murmur was heard at the apex. There was no diastolic murmur. The first sound at

the apex was reduplicated. There was absolute arrhythmia. He was given digitalis from a carefully assayed lot. He left the clinic saying that he and his wife were contemplating a trip to Europe, and he would report to us again on his return in the fall. His electrocardiogram at this last visit was essentially the same as Fig. 214.

Discussion of Case II.—In this case we can watch the development of variations in the electrocardiographic curve over a period of six years. A slow downward clinical progress, including the onset of auricular fibrillation, in an old man with marked arteriosclerosis, has been accompanied by progressive changes in the form of the initial ventricular complex of the electrocardiogram. The changes took the form of widening, variation in amplitude, and notching. It is worth noting that the most considerable change took place in the eleven months which elapsed between the tracings shown in Figs. 211 and 212, and that this change was greater than that occurring in the succeeding five years. The change in this case is permanent and progressive; it must then be associated with and due to a permanent and progressive change in the conducting system. The assumption, based upon the pathologic investigations of Oppenheimer and Rothschild⁴ and others, is that there has been in this patient's heart a progressive sclerotic change involving the conduction system. Lewis¹⁵ has stated that degenerative influences tend to act selectively on these specialized tissues. A case of heart-block was studied for two years by Karfunkel,¹⁶ who observed changes in the degree of block and changes in the QRS complex during that period. The changes in the configuration of the electrocardiogram in the case just described are associated with changes in rhythm and with a slowly downward clinical progression.

Case III.—M. T. West Medical. 208.935. Cardiosclerosis. Adherent Pericardium. Perihepatitis. Auricular Fibrillation. Bundle Branch Block. Heart Failure.—This patient is a white male, born in Austria sixty-eight years ago. He has always worked as a tailor.

He was first seen about seven years ago. For eight years previous to his first entry he had suffered from "asthmatic

attacks," usually associated with wet weather and characterized by cough, dyspnea, and orthopnea. For two months he had been very weak, had had the symptoms he associated with his "asthmatic attacks" and, in addition, some epigastric discomfort. His legs and feet had been swollen for two weeks.

His family history was unimportant. In his past history he denied venereal disease and any type of rheumatic infection. He was accustomed to two small glasses of brandy daily.

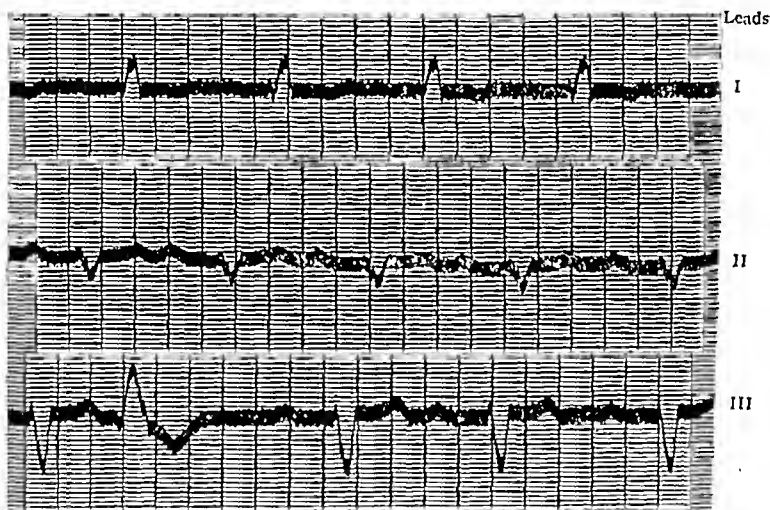


Fig. 215.—Case III. February 9, 1915. Partial heart block (P-R interval 0.3+ second). "Right" bundle branch block. A ventricular premature beat. Notching of QRS complex in all leads.

Examination revealed marked arteriosclerosis. His heart was enlarged, the apex in the sixth space 13 cm. to the left of the midline. The sounds were of poor quality. There were systolic murmurs only. There was moderate ascites. The edge of the liver was felt 6 cm. below the costal margin. Blood-pressure 125/70. The pulse-rate was not rapid, varying between 70 and 80. There was no fever. The Wassermann test was negative; the luetin test positive. His recorded diagnosis was hepatic cirrhosis, ascites, hypertrophy and dilatation of the heart, cardiac asthma, and possibly syphilis.

Eight months later he re-entered the wards with a five-day history of cough and hemoptysis. A polygram at this time showed alternation and occasional ventricular premature beats. The Roentgen ray demonstrated that the shadow of his heart was 17.3 cm. and that of his great vessels 7 cm. in diameter.

Other entries follow, with nearly identical stories. In February, 1915 an electrocardiogram was obtained (Fig. 215). It showed a long P-R interval (0.3+ second), "right" bundle branch block, a ventricular premature beat, and deep notching of Lead II. In November, 1915 his auricles began permanently to fibrillate.

In April, 1916 he entered the wards, complaining, in addition to the usual symptoms of his periodic decompensation, of a distended belly, and announcing that he had been tapped once some four months before. Since then tapping has been necessary at constantly decreasing intervals, until now (1921) the interval is only two weeks. His phenolsulphonephthalein output in 1916 was 20 per cent. in two hours. His clinical diagnosis was: adherent pericardium, myocardial degeneration, auricular fibrillation, right bundle branch block, perihepatitis, and ascites.

Since then he has been followed in the Cardiac Clinic. His progress has been slowly but definitely downward. In spite of continuous digitalis therapy, which relieves him somewhat, he has for years been constantly dyspneic, edematous, and cyanotic.

In November, 1920 he was seen at the Cardiac Clinic. He complained, as always, of weakness, dyspnea, orthopnea, and a swelling belly. His pulse-rate was 60, with no deficit. The apex-beat was seen and felt in the seventh intercostal space in the midaxillary line. There was a blowing systolic murmur over the precordia. No diastolic murmur was heard. The chest was hyperresonant; râles were heard at both bases. There was edema of sacrum and shins. Ascites was marked, and cheeks, lips, and finger-nails showed very marked cyanosis. His lips were almost black. His electrocardiogram at this time (Fig. 216) showed auricular fibrillation and notable changes in the form of the QRS complex. Lead I showed a reduction in the magni-

tude of the initial ventricular complex and deepening of the notching; Lead II remained about the same; Lead III exhibited some new upward deflection, a diminished downward deflection, and deepened notching. The T waves remained opposite in sign to the initial ventricular complex.

Discussion of Case III.—This patient showed severe interference with conduction at the time of his first tracing in 1915. Since then his auricles have begun to fibrillate, and his QRS complex is considerably changed, while his clinical condition has

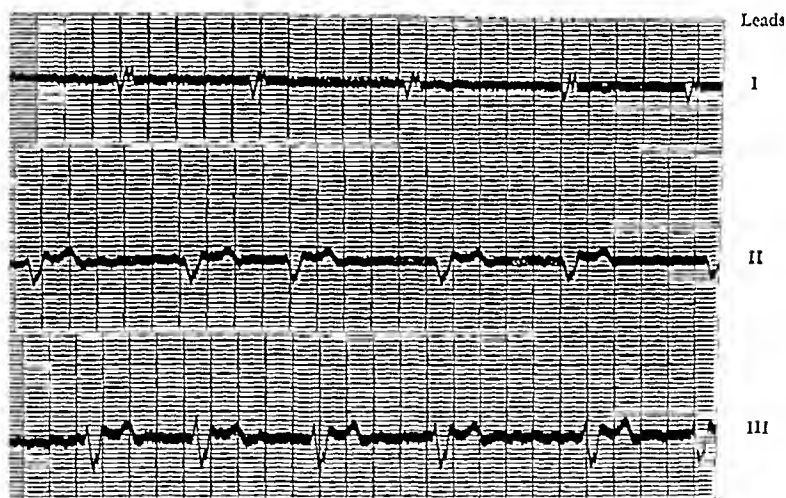


Fig. 216.—Case III. November 10, 1920. Auricular fibrillation. QRS complex smaller and more notched in Leads I and III than in former tracings.

slowly altered for the worse. At present (May, 1921) he exhibits symptoms of profound heart failure; he is confined to his house and will probably not live many more months. His electrocardiogram does not now resemble the curves typical of bundle branch block, but is more like those described by Oppenheimer and Rothschild⁴ as a type of intraventricular block. There seems no reason, theoretically, why bundle branch block and arborization block should not exist together, especially in a case such as this, in which previous electrocardiograms have indicated

the presence of bundle branch block. In this case, as in the previous one, we see slowly progressive failure associated with changes in the initial ventricular complex.

Case IV.—A. L. East Medical, 212,094. **Cardiosclerosis. Chronic Nephritis. Glycosuria. Cardiac Enlargement and Failure.**—The electrocardiographic study of this patient was begun in April, 1915. At that time he was sixty-five years old. He had done no work for years. The hospital record goes back to 1908, when he had been treated in the Out-patient Department for "nephritis" and "diabetes." For some fifteen years before his entry in 1915 he had had polyuria, polydipsia, and an excessive appetite. During this same period he had been so short of breath as always to sleep on several pillows. At intervals of a few months he would become increasingly dyspneic, fill up with edema, and require hospital care. At these earlier admissions his glycosuria cleared promptly; rest, diet, and digitalis would markedly improve his cardiac and renal conditions and he would be discharged in fairly good condition. But he inevitably broke his regimen, and as inevitably suffered for it.

Just before his entry in 1915 he had been fairly well for some months. A fortnight before his admission he began to experience increasing dyspnea, palpitation, and precordial pain. His feet swelled and in two weeks he gained 15 pounds in weight.

His early history was essentially negative.

Physical examination showed an obese old man, slightly cyanotic, dyspneic, orthopneic, and talkative. His pupils were irregular and reacted sluggishly. Both lung bases were dull and exhibited moist râles and diminished breath sounds. By percussion his heart was 5 cm. to the right and 17 cm. to the left of the midline. The supracardiac dulness measured 8 cm. The heart sounds were distant; the aortic second greater than the pulmonic second. A blowing systolic murmur was heard over the precordia. His blood-pressure was 200/120. His radial arteries were easily palpable. There was brawny edema of legs and thighs, and some slighter swelling of his hands. Examination of urine revealed a trace of albumin, a trace of sugar, and many hyaline and granular casts. Phenolsulphonephthalein

excretion was 30 per cent. in two hours. Wassermann on the blood was negative. An electrocardiogram at this time (Fig. 217) showed "right" bundle branch block, a slurring of the initial ventricular complex in Leads I and III, and a notching in Lead II. The P-R interval approached 0.2 second. A diagnosis of arteriosclerosis, chronic nephritis, myocardial insufficiency, hypertrophy and dilatation of the heart, and glycosuria was made. He was bled, purged, and dieted, and lost 36 pounds, with great subjective improvement.



Fig. 217.—Case IV. April 2, 1915. "Right" bundle branch block. Notching of R-wave in Lead II. Slurring in Leads I and III. P-R interval increased over normal.

A year later (March, 1916), after again lapsing from his diet, he entered the wards in much the same condition. He had perhaps more edema, and his phenolsulphonephthalein excretion had fallen to 12 per cent. He showed at this time three distinct cardiac mechanisms: (1) periods of normal rhythm plus many premature beats, both auricular and ventricular; (2) paroxysms of auricular fibrillation; and (3) paroxysms of tachycardia. The tracing illustrated in Fig. 218 was taken during one of the paroxysms of tachycardia. The QRS complexes are of much

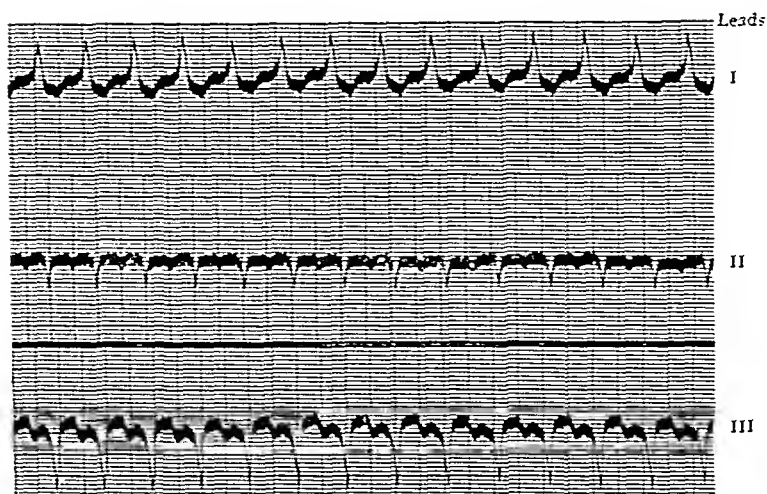


Fig. 218.—Case IV. March 28, 1916. Paroxysmal tachycardia. QRS complex has changed but little. Patient acutely decompensated.

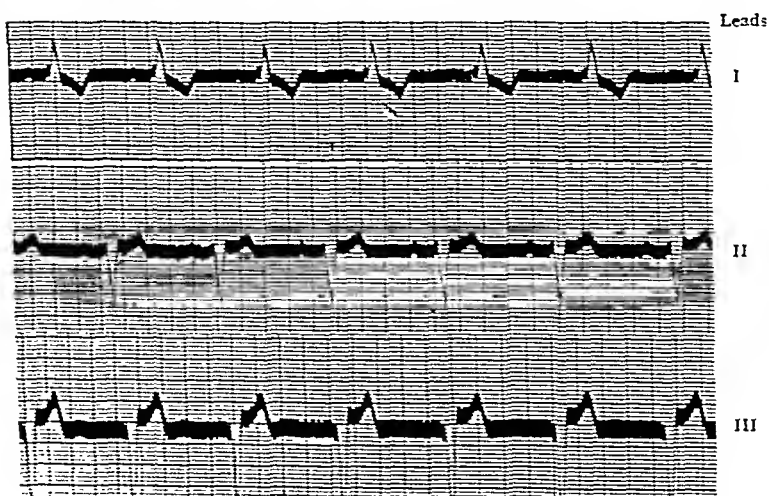


Fig. 219.—Case IV. April 17, 1916. During period of normal rhythm, when there was no serious heart failure. The notching in Lead II is less and in Lead I more distinct.

the same type as before, except that the notching is perhaps a little deeper than in the previous year. This plate was taken

while the patient was still decompensated. A curve obtained just before his discharge, however (Fig. 219), showed a considerable variation from the curve of a year before. The amplitudes of the deflections in Leads II and III were greater and the notching in Lead II much less distinct. In Lead I the notching was more distinct.

In December, 1916 he again entered the wards, very cyanotic, with pulmonary edema and an engorged liver. The usual measures failed, and he died. His final tracing (Fig. 220) was

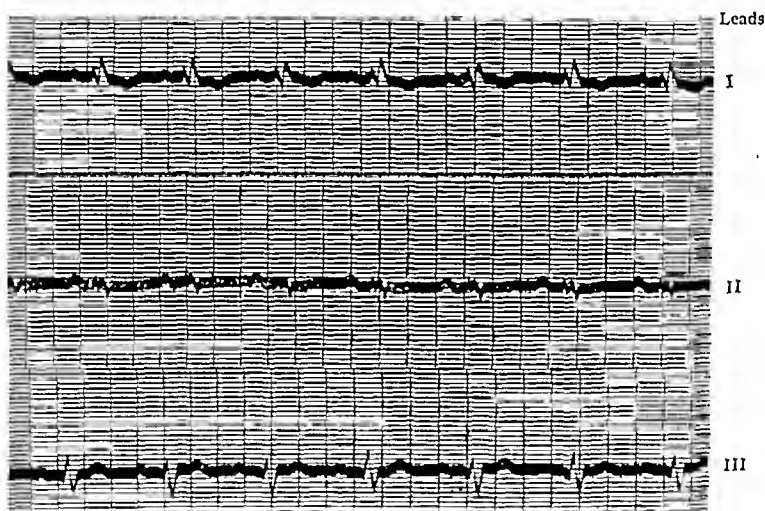


Fig. 220.—Case IV. December 7, 1916. Acute decompensation three days before death. Diminution in extent of excursion. Increased notching.

obtained only three days before his death. The shape of the initial ventricular complex had undergone a profound change. The picture was no longer typical of bundle branch block alone, but undoubtedly a more wide-spread interference with conduction and resultant aberration had supervened.

Discussion of Case IV.—This patient had a long history of cardiac and renal disease based upon arteriosclerosis. His first electrocardiogram exhibited disturbances of conduction, and in the twenty months which elapsed before his death he developed

not only changes in rhythm but also further variations in the configuration of the initial ventricular complexes. Just before he died his curve showed the most marked variation, losing its resemblance to the typical curve of bundle branch block. This association of maximal variation with severe decompensation suggests that these final disturbances of conduction were due to an acute injury.

Case V.—J. F. G. East Medical, 241,128. *Cardiosclerosis. Auricular Flutter and Fibrillation (Paroxysmal). Heart Failure.*—This patient is a white male, sixty-four years old, and

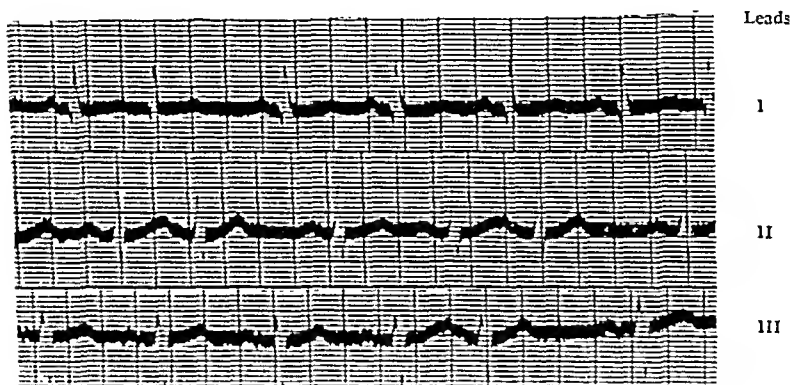


Fig. 221.—Case V. December 31, 1914. Left ventricular preponderance. Auricular premature beats.

formerly worked as a machine operator in a shoe factory. He was first seen by us in December, 1914. At that time he weighed 263 pounds, and reported that a few years before he had weighed 320 pounds. He gave no history of rheumatic or venereal infection. He had always been well and strong up to the time of his entry into the hospital. His chief complaint was increasing weakness and great fatigability. He was short of breath and accustomed to sleep on two pillows. Physical examination demonstrated cyanosis of lips and edema of feet and ankles. His heart sounds were distant; there was nothing to suggest valvular disease. His electrocardiogram (Fig. 221) exhibited

left ventricular preponderance (which is quite explicable on the score of his great weight and its accompanying transverse heart) and auricular premature beats. The QRS complex was of normal duration and outline.

In spite of long periods of rest, the constant administration of digitalis, and loss of some of his weight he progressed slowly downward. In 1919 he was acutely decompensated and in the wards of the hospital for three weeks. Since then he has

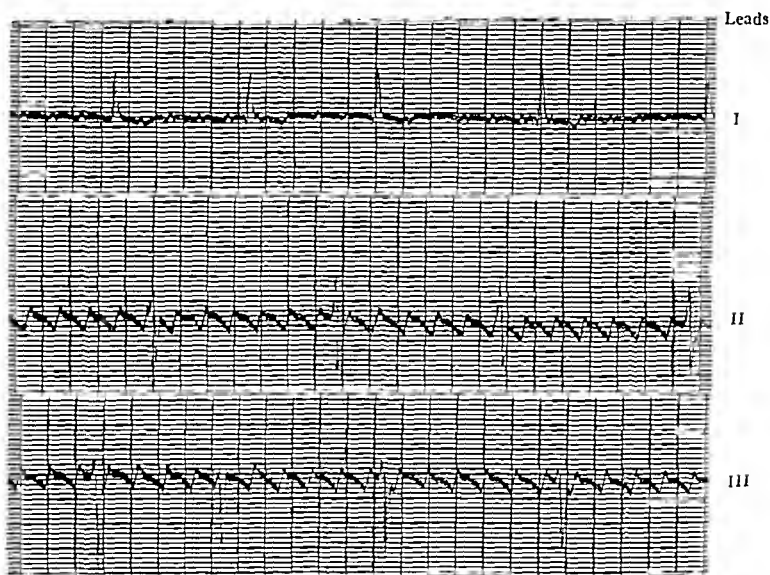


Fig. 222.—Case V. January 24, 1921. Auricular flutter. Varying degrees of A-V block. Ventricular complex as before.

done no factory work, but has spent his time doing housework for himself and his sister.

In January, 1921 he appeared in the Cardiac Clinic complaining of increasing dyspnea and weakness. He was found to have auricular flutter, with an auricular rate of 300, and a varying degree of A-V block. Under thorough digitalization his auricles began to fibrillate, and upon withdrawal of the drug returned to normal rhythm, interspersed with many ectopic beats. He

is now very limited in the range of his activity. Figure 222 is an example of the electrocardiograms taken at this time. It showed auricular flutter and otherwise very nearly the same things that it had shown six years before. The QRS complex, in particular, was of essentially the same form.

Discussion of Case V.—This last patient illustrates another side of the story. Although observed for over six years and having a definitely downward clinical course and exhibiting at various times flutter, fibrillation, and showers of premature beats, his QRS complex remained very nearly constant. The obvious assumption in explanation of this difference is that the progressive sclerotic change has in his case produced no extensive damage to the conducting tissues, although almost certainly involving considerable areas of muscle. Drury¹⁷ has described an interesting case in which "wide-spread fibrosis consequent upon closure of the descending branch of the left coronary artery" was accompanied by a normal electrocardiogram.

Summary and Conclusions.—A short series of cases has been described illustrating various types of deformity of the QRS complex of the electrocardiogram. Four of these cases have been followed for periods of years, and in this way it has been possible to study the development of variations from the normal configuration.

It has been laid down that departure from a type of curve normal for a given individual is contingent upon departure of the excitation wave from its normal pathway, and that this pathway is determined by the architecture and functional ability of the conduction system. Thus, changes in the QRS complex are transient if the conduction changes which cause them are transient (Case I), and are permanent if there are definite organic changes interrupting the conducting fibers. It is probable that in most cases both factors are at work.

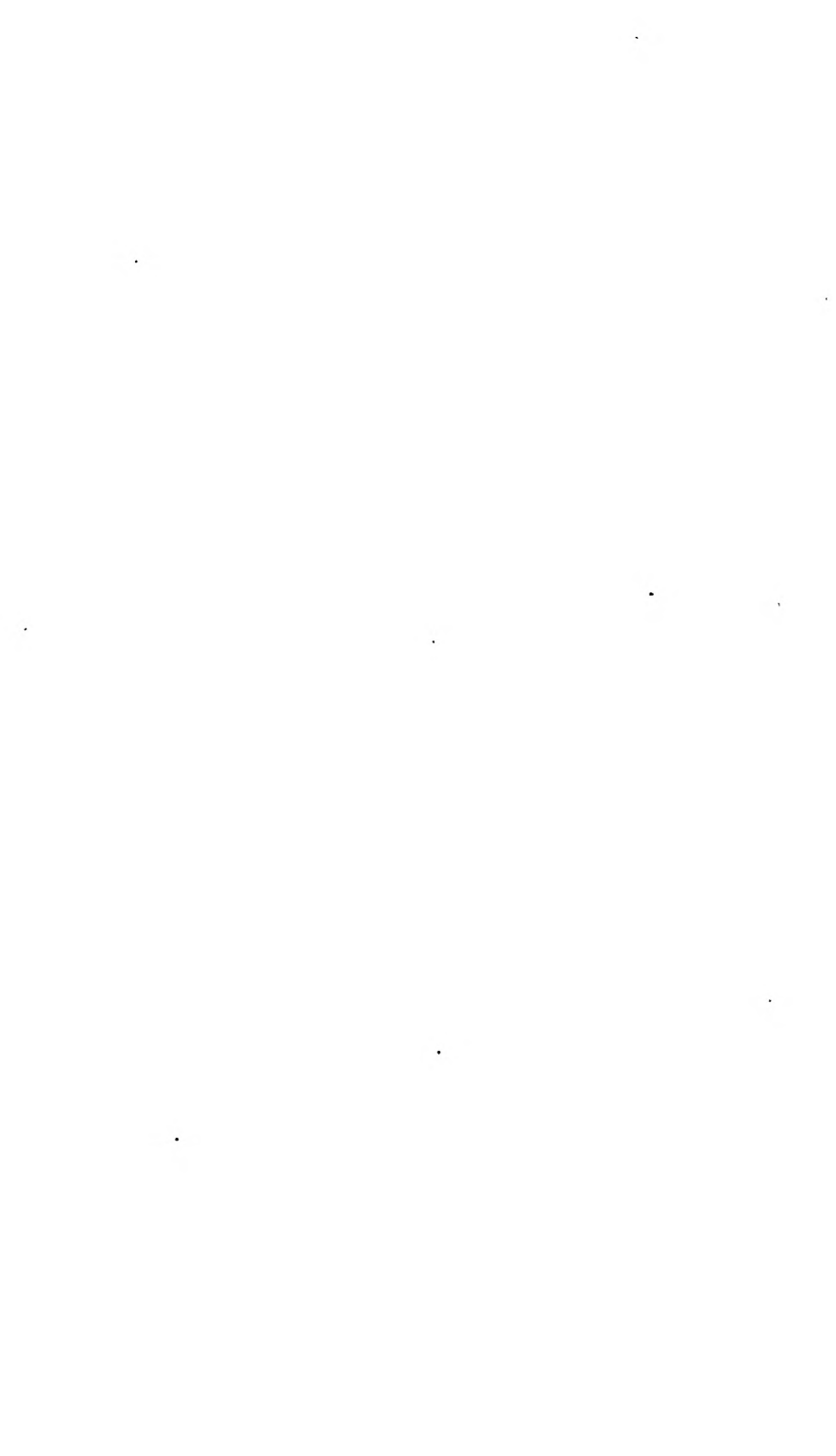
Cases which have shown progressive change in their initial ventricular complexes have shown a progressive change downward in their clinical conditions. Case V suffered a clinical change comparable to that of the others, but the QRS complex remained of normal outline, demonstrating that severe impair-

ment of cardiac function may be associated with a normal ventricular complex, probably in the absence of extensive damage to the conduction system. The degree of change in the electrocardiogram was not parallel to the clinical evidence of cardiac damage. Arteriosclerosis was apparently the cause of the progressive cardiac involvement in these cases.

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SOME NEUROLOGIC ASPECTS OF CHOREA

MOST authors in discussing chorea consider it only from the infectious or endocarditic standpoint, and fail to bring out the striking neurologic aspects of the disease. This case is presented to emphasize these neurologic aspects:

A. S., nine years of age, male, was admitted to the service of Dr. F. B. Talbot on March 28, 1921, with a diagnosis of chorea and rheumatic heart disease.

Family History.—Father, mother, and two brothers living and well. One child died of diarrhea at five weeks. One brother was admitted to this hospital November 27, 1920 with a diagnosis of polyneuritis; discharged with a questionable diagnosis of trichinosis and pediculosis capitis. No miscarriages or history of exposure to tuberculosis. No insanity. Mother is deaf, possibly feeble-minded. Father is a nerve case; was at the Psychopathic Hospital for ten days, complaining of jealousy, suspicion, and timidity. His Wassermann was negative.

Past History.—Except for malnourishment the patient was well until last September, when he was admitted to this hospital with a septic knee (right) due to a puncture wound. He was discharged after five days to the Out-patient Department. On February 3, 1921 he reported at the O. P. D., complaining of pain in his groin, legs, and left arm. Examination was negative except for muscular weakness. He was referred to the Infantile Clinic, and they note: "The absent knee-jerk, pain, and weakness in abductors of right thigh and arm are the only signs of poliomyelitis. No paralysis. May be anterior poliomyelitis; brother had similar condition in November, 1920." Advised

to enter house for observation, but no bed was available, so he returned to his home. The pain and weakness disappeared, but recurred whenever he got his feet wet.

Present Illness.—Three weeks ago his teacher noticed that he could not stand still. School work began to tire him and the teacher says that in her opinion "the boy is crazy." When seen in the O. P. D. today (March 28th) he showed marked chorea, with almost complete lack of control. Temperature 101° F. Heart conspicuously enlarged.

Physical Examination.—A fairly well-developed, poorly nourished Italian boy. He shows marked choreic movements of whole body.

Skin: Warm, smooth, and dry.

Reflexes: Pupils equal and react to light. Neck not stiff and no neck sign. Abdominal and cremasteric reflexes are lively and equal. Knee-jerks normal. No Kernig or Babinski and no clonus.

Head: Bosses prominent; site of anterior fontanel depressed; scalp clean, no nits or pediculi seen.

Eyes: No discharge; conjunctivæ slightly injected; cornea and scleræ clear; no recession.

Ears: Slightly pointed; drums not red; no bulging.

Nose: Normal shape; slight mucous discharge and slight obstruction on right.

Mouth: Gums pale; teeth irregular; malocclusion, two deciduous incisors present and loose. Dentition delayed. No Koplik's spots.

Throat: Fauces pale; tonsils probably have been removed, but there is a small amount of tonsillar tissue yet in the fossæ. No adenoids, no stridor.

Lymph-nodes: At angles of jaw there are three or four glands of the size of a large bean; posterior cervicals are palpable; axillary and inguinals are the size of a small bean; epitrochlears palpable on right.

Thorax: Slightly flaring; beading still palpable; slight rosary.

Lungs: Resonant throughout; no râles, breath sounds normal.

Heart: Borders 2.5 cm. to right of midsternal line and 10

cm. to left. Apex 8 cm. to left out, 1 cm. outside nipple line in fourth space. Murmurs: At apex soft systolic blowing murmur transmitted to axilla; no diastolic murmur; first sound seems rather muffled, with the second prolonged; at the base the first pulmonic sound is replaced by a harsh, high-pitched murmur, the second is accentuated, short, and sharp; first aortic is not well heard, second aortic faint. Pulmonic second sound is louder than aortic second. Rhythm and force fair.

Abdomen: Flat, no masses, no tenderness; liver palpable at costal margin; spleen not felt. Genitals: No discharge; testicles in scrotum. Buttocks: Not red; rectal not made.

Laboratory Examinations.—The urine on eight examinations was negative except for a slight trace of sugar twice and an occasional white blood-cell.

Blood (March 28th): W. B. C., 10,300; Hgb., 75 per cent.

Smear shows: Polymorphonuclear cells, 49 per cent. Lymphocytes, 45 per cent. Large mononuclears, 5 per cent. Eosinophils, 1 per cent.

On April 3d: W. B. C., 13,000.

Smear shows: Polymorphonuclear cells, 60 per cent. Lymphocytes, 26 per cent. Large mononuclears, 13 per cent. Eosinophils, 1 per cent.

Wassermann reaction negative.

Blood-pressure 112 systolic, 55 diastolic.

The stool examination was negative.

The Von Pirquet test was negative.

The Schick test was twice negative.

The electrocardiogram showed: Rate, 80; marked sinus arrhythmia; normal mechanism, no preponderance.

On April 6th a special heart examination showed a change in condition as follows: Impulse 7.5 cm. out; slow; respiratory arrhythmia; soft apical systolic murmur not masking the first sound; third heart sound present; no definite evidence of heart involvement. Potential heart disease. Chorea is much improved. Advise clearing up of foci of infection in mouth.

We have, then, a quite typical case of chorea running a sub-acute course with slight fever, a history of arthritis, and finally

slight endocarditis, with enlargement of the heart. These have improved under treatment.

By going through a careful neurologic examination we can bring out the following points:

In the first place we observe the boy as he lies stripped, and notice that he frequently performs *purposeless inco-ordinate movements* of short duration. Most of these movements are in the right upper extremity, but some are in the right leg and on the left side. There are also grimaces of the face and sudden winkings of the eyes. These are the typical involuntary movements of chorea. It is remarkable how few good descriptions of these are to be found in medical literature. Perhaps the best is Osler's in his monograph.¹ Other descriptions well worth reading are those by Weir Mitchell² and by Russell.³

Next let us test the muscular co-ordination. We observe that when asked to perform a simple act he is able to largely inhibit the choreic movements and exhibits good muscular co-ordination. There is at times a little difficulty in making movements he intends to make; there is more involuntary movement when he tries to lie quiet with all of us observing him. In other words, there is nothing of "intention tremor" in the phenomenon. But there are certain inco-ordinations—not marked inco-ordination of voluntary movement, but *lack of normal association* of simple movements. For example, we ask the patient, while lying supine, to fold his arms on his chest; we then command him to sit up. In his struggle to do so the right leg flies up from the bed, while the left leg presses firmly down into the mattress. This is the "second sign of Babinski" and shows that the proper motor associations of the right leg, thigh, and trunk muscles are not present.⁴ There is a motor dissociation, more marked on the right side. It is interesting to note that this is the side most affected by the involuntary twitches.

In many cases of this disease only one side of the body is affected. These are the so-called "hemichoreas," and they show "Babinski's second sign" conspicuously.

Another motor abnormality is easily elicited by telling the patient to grip your fingers with his hand firmly and steadily.

If he has a marked chorea you can readily feel the instability of his grip. That is to say, the patient is unable to maintain a steady muscular contraction. Dr. L. F. Barker has brought out this point in his clinics, and, to my mind, it is the most constant neurologic sign of the disease. Electromyograms showing this *failure of the ability to maintain tonic contraction* have been made, and they graphically record that a patient ordered to grip a dynamometer steadily cannot do so.⁵

The tendon reflexes in this case are present and equal on the two sides. The abdominal and cremasteric reflexes are normal, and plantar stimulation causes plantar flexion of the toes. In other words, the "Babinski is negative." Thus we have no evidence of a lesion of the pyramidal tract or any part of its course. But many cases at certain times show a "Babinski" in one or both feet, and there is often *weakness* of the extremities, most conspicuous in hemichoreas. The only other positive findings in our routine neurologic examination are concerned with the vocal organs, tongue, and facial expression. The *speech* is lacking in expression; it is monotonous, but irregular and explosive at times. Swift considers that there is a definite voice sign in chorea.⁶ The facial expression is silly and indicates *mental* deficiency. In this case the mother is said to appear feeble-minded, and the father has been recently in a psychopathic hospital, so it may well be that the patient is congenitally defective. But it is not uncommon for previously bright children to be dull, and some bad cases become extremely restless, sleepless, and even go into acute deliria. It would be well to look up the school record of this child, and during his convalescence to test his mental level by the Binet scale.

The question of the mental or "functional" factors in this disease have often been discussed. Osler⁷ says: "One theory is that chorea is a functional brain disorder. The predominance of the disease in females, and its onset at a time when the education of the brain is rapidly developing, are etiologic facts which Sturges has urged in favor of the view that chorea is an expression of functional instability of the nerve centers. . . . Lately chorea has been regarded as an infectious disease. One objec-

tion to this theory is that there can be no doubt that ordinary chorea may rapidly follow a fright or a sudden emotion."

This whole subject is an obscure, but interesting one. Can an organic lesion, previously without overt symptoms, be suddenly made active by an emotional shock? There are so many cases on record where this seems to have occurred that we must consider it as a reasonable possibility, although the physiologic and pathologic mechanisms are not understood. We know that thyrotoxicosis may come on suddenly after a fright, with all the symptoms of Graves' disease. This is perhaps an unfair comparison, for we know something of the relation of the emotions to the endocrine glands through Dr. Cannon's work.⁸ But it is not a great step farther to explain in some analogous way such strange occurrences as the sudden onset of the symptoms of Friedreich's ataxia in a patient after being thrown into a river by robbers (a case which was at first considered hysteria, of course, but was later proved at autopsy to be Friedreich's ataxia). This subject must, at present, be left in the stage of mere hypothesis. Many cases of adult chorea are undoubtedly mental, and it is interesting that a good history almost always elicits that the patient had chorea as a child. The probable explanation of this is that the mental anguish of living through a period of lack of motor control leaves on the personality an indelible impression, so that in later life, if this individual is to have a psychosis, it may more easily take the form of chorea than any other type of symptomatology. The chorea of pregnancy and the puerperium fall into this group; but any severe emotional strain might bring out the same reaction in a predisposed individual.

If we can thus explain the cases that are psychogenic, what is the anatomic basis in the organic cases? Osler⁷ in 1911 said: "No constant lesions have been found. Embolism of the smaller cerebral vessels has been found. Endocarditis is by far the most frequent lesion in Sydenham's chorea. With no disease, not excepting rheumatism, is it so constantly associated. The embolic theory has a solid basis of fact, but it is not comprehensive enough. There are instances without endocarditis and

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SUBDIAPHRAGMATIC INFLAMMATORY CONDITIONS

It is well recognized that pulmonary and pleural lesions may give rise to abdominal symptoms. The abdominal pain in lobar pneumonia, particularly in children, is classical, and when the pain is on the right side the differential diagnosis between lobar pneumonia and acute appendicitis is always referred to in the text-books. However, it is not so well recognized that abdominal lesions may give rise to thoracic symptoms. To be sure, there is the classical example of the referred pain of gall-stones which is mentioned in every text-book. Experimental and clinical work has, however, brought out the fact that involvement of the diaphragm may well be associated with the symptoms ordinarily attributed to the lungs and pleuræ. Abdominal lesions, that is to say, lesions below the diaphragm, may cause not only symptoms but also clinical signs that are thoracic in the usual sense. Clinicians recognize somewhat vaguely that tumors of the upper abdominal organs may extend into the so-called thoracic cavity. It is much less well recognized that temporary tumors, such as inflammatory processes and the enlargements of the spleen, may produce the same picture. The confusion is entirely due to the fact that the diaphragm is a rather widely moving curtain, and that, as Picqué emphasized in 1910, a collection of pus underneath the diaphragm of abdominal origin would be in the same cross-section as a collection of pus above the diaphragm of pulmonary or pleural origin. Picqué objects to the exclusion of subdiaphragmatic abscesses from the category of thoracic empyemata. High abscesses below the diaphragm are actually within the

and published the case of a ten-year-old girl dying of a typical acute chorea on the tenth day of her disease. The autopsy showed a polio-encephalitic process especially conspicuous in the corpus striatum, and involving somewhat the cortex, thalamus, and pons. This distribution is similar to that found in the chronic chorea of Huntington, but the lesions are acute and histologically indistinguishable from those of lethargic encephalitis. It is interesting that the recent pandemic of encephalitis lethargica has given us many examples of choreiform movements in infectious disease, and the predilection of this form of encephalitis for the basal ganglia is well known.

We are beginning, therefore, to get evidence which gives us a concrete conception of the anatomic and physiologic pathology of this disease, first accurately described by Sydenham two hundred and thirty-five years ago, and ever since then a puzzle to clinicians and pathologists.

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the diaphragm. It has been our experience repeatedly that a pain in the region of a subdiaphragmatic inflammation has been entirely overlooked as being rather too indefinite and, furthermore, that not infrequently tenderness which was not suspected turns out to be very definite when looked for. It is perfectly true that there is a tendency to disregard elsewhere in the body the amount of pain and tenderness which located in the abdomen would give rise to grave concern. While pain and tenderness do not have everywhere the same importance, nevertheless they should be more carefully considered than they are at the present time. The pain may resemble a low pleuritic pain. In subdiaphragmatic inflammations the tenderness is naturally apt to be located near the site of the inflammation. By percussion one derives the most valuable information. It will be found, due to the fact that the diaphragm is held high and rigid, that there is general dulling of the percussion note on the affected side. By very light percussion it is possible to percuss the top of the diaphragm and, when the breathing is quiet, it will be found that the top of the diaphragm will be higher on the affected side than on the normal side. On the other hand, if the pleural cavity is not involved the lower margin of the diaphragm will be in the normal position on both sides. If the inflammatory process is not particularly acute, and is not in close proximity to the diaphragm, it not infrequently happens that forced inspiration will cause the diaphragm to undergo a normal excursion. Precisely the same phenomenon can be seen with the x-ray. It is of considerable importance that the patient be examined during quiet breathing in order that one may be able to demonstrate the diaphragm in the position that it has taken in consequence of the inflammation, which position may be varied, as I have said, by forced breathing. It will be seen that the procedure is nothing more or less than determining the highest and the lowest levels of the diaphragm. This is done posteriorly for obvious reasons. For many years we have been accustomed to ascertain the dome of the diaphragm on the right side in front in order to obtain the upper border of the liver. It apparently is not practised, nor is it recommended

limits of the bony cavity of the thorax. Picqué would have us designate such abscesses as occur within the limits of the bony thorax as thoracic abscesses, with a further designation of the position of the abscess in regard to the diaphragm, as well as any other descriptive anatomic or bacteriologic terms. Such a viewpoint has much to recommend it.

In 1915 I was able to collect 4 cases of subdiaphragmatic inflammation, all of which were at first mistaken for pleural or pulmonary conditions and all of which went on to spontaneous recovery. The interest aroused by this small series of cases has continued and has emphasized the validity of Picqué's suggestion, and has led to the collection of a considerable series of cases of inflammation just below the diaphragm. These conditions are of wide and varied etiology, and they do not resolve themselves easily into particular groups from the point of view either of anatomic situation or of bacteriologic origin. The commonest general group is that one known as perinephric abscesses which in the early stages are often obscure.

The key to the situation is the determination of the level of the diaphragm in regard to the pathologic process. To the x-ray we owe our present ability to interpret accurately physical signs in relation to the diaphragm. I do not mean that a diagnosis can only be made by the x-ray. I mean that the x-ray has enabled us to check up our observations in regard to the precise location of the diaphragm, and that by accumulating these observations we are now in a position to make accurate deductions from clinical findings alone without the assistance of the x-ray. It is, I believe, a confession of weakness that one must always depend upon the x-ray for very precise diagnoses. In some of our cases the x-ray has been somewhat confusing. Furthermore, when the x-ray technic was being developed, occasionally the clinical diagnosis would outstrip the x-ray diagnosis.

The same general tendencies and reactions hold true in thoracic inflammation as in inflammations elsewhere. One has to a varying degree the classical symptoms of pain, tenderness, and rigidity. This is particularly true in lesions below

the diaphragm. It has been our experience repeatedly that a pain in the region of a subdiaphragmatic inflammation has been entirely overlooked as being rather too indefinite and, furthermore, that not infrequently tenderness which was not suspected turns out to be very definite when looked for. It is perfectly true that there is a tendency to disregard elsewhere in the body the amount of pain and tenderness which located in the abdomen would give rise to grave concern. While pain and tenderness do not have everywhere the same importance, nevertheless they should be more carefully considered than they are at the present time. The pain may resemble a low pleuritic pain. In subdiaphragmatic inflammations the tenderness is naturally apt to be located near the site of the inflammation. By percussion one derives the most valuable information. It will be found, due to the fact that the diaphragm is held high and rigid, that there is general dulling of the percussion note on the affected side. By very light percussion it is possible to percuss the top of the diaphragm and, when the breathing is quiet, it will be found that the top of the diaphragm will be higher on the affected side than on the normal side. On the other hand, if the pleural cavity is not involved the lower margin of the diaphragm will be in the normal position on both sides. If the inflammatory process is not particularly acute, and is not in close proximity to the diaphragm, it not infrequently happens that forced inspiration will cause the diaphragm to undergo a normal excursion. Precisely the same phenomenon can be seen with the x-ray. It is of considerable importance that the patient be examined during quiet breathing in order that one may be able to demonstrate the diaphragm in the position that it has taken in consequence of the inflammation, which position may be varied, as I have said, by forced breathing. It will be seen that the procedure is nothing more or less than determining the highest and the lowest levels of the diaphragm. This is done posteriorly for obvious reasons. For many years we have been accustomed to ascertain the dome of the diaphragm on the right side in front in order to obtain the upper border of the liver. It apparently is not practised, nor is it recommended

by the text-books that the same procedure be carried out posteriorly where it is capable of eliciting information of great value. Of course, there are difficulties in interpretation. A thickened pleura will give abnormal dulness, but, as a rule, the limited excursions, even of a high fixed diaphragm, will be sufficient to differentiate that condition. The presence of fluid is differentiated from the high diaphragm by the fact that fluid raises the lower level of dulness.

It sometimes happens that the dome of the diaphragm is elevated on both sides, and consequently we have difficulty in making a comparison with the normal. The usual level which experience has taught us to take as the top of the diaphragm in quiet breathing is a point just above the angle of the scapula on both sides, and this will be higher on the right side than on the left.

When the subdiaphragmatic process is associated with fluid one runs into difficulties from which not even the x -ray may be able to extricate us. There is generally the x -ray evidence that the diaphragm is high and that the fluid accumulation is comparatively slight. In such an event it is important that some of the fluid be obtained for examination. As a matter of fact, that fluid is often obtained with great difficulty. That in itself is of some importance in denoting that while the clinical signs and even the x -ray signs may point to considerable effusion, a sample of that effusion shows it to be scanty and the diaphragm is probably high. In our experience the fluid shows the characteristics of an exudate. It is often not unlike the typical fluid of tuberculous fluid with a large amount of albumin and the specific gravity of approximately 1020. Polynuclear cells usually predominate. Nevertheless occasionally, as in one case, the specific gravity was 1022, there were 800 cells per cmm., of which 91 per cent. were mononuclear cells. The important feature of the examination of the fluid is the bacteriologic examination. If in the presence of the general signs of acute inflammation the fluid above the diaphragm is sterile, the evidence is strong that the essential process is below the diaphragm, and that the fluid above the diaphragm does not

represent an acute bacterial extension, but what we designate as an irritative non-septic fluid.

It has been my desire to discuss the general problem of diagnosing inflammatory processes below the diaphragm. I have tried to outline some of the essential features which are concerned, and would particularly lay stress upon the fact that there are subdiaphragmatic conditions which simulate closely in signs and symptoms conditions above the diaphragm. The contention that the diaphragm because it is a widely moving curtain does not make as real a subdivision in the thoracic cavity as once thought seems to be sound. After all, the pathologic process is in the same situation in an imaginary cross-section of the thorax, irrespective of whether the process is above or below the diaphragm. From a practical point of view it is of the greatest importance to determine whether such a process is above or below the diaphragm. Consequently, the determination of the level of the diaphragm, which means the top of the diaphragm, becomes of paramount importance. It is to this feature that I particularly commend your attention.



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TYPHUS FEVER¹

TYPHUS fever is a disease of which, through the good fortune of our country, American physicians have little first-hand knowledge. Few cases have occurred in American communities during the last half a century. In the important European clinics for postgraduate instruction during the decades preceding the Great War the disease was infrequent. Thus probably a great majority of the physicians of this country have never seen a case, and few have seen enough cases to acquire a familiarity with the course of the disease.

Yet, as all who read the daily papers must know, epidemics of typhus fever which broke out in East-central Europe in the course of the war are still raging in spite of preventive measures undertaken on a large scale to control them. There is real danger that the disease may spread along channels of emigration and start new epidemics in susceptible communities still uninfected. Already it is reported that cases have been discovered on immigrant ships arriving in America. There is therefore no certainty that typhus may not sooner or later gain a foothold with us in louse-infested communities.

Historically, typhus fever owes its importance to its tendency to break out in epidemic form in the train of wars, famines, and other social catastrophes that result in destitution and

¹ The observations upon which this description is based were made in the course of the work of the Typhus Research Commission of the League of Red Cross Societies at the St. Stanislaus Hospital, Warsaw, Poland, February-June, 1920.

crowding of populations. While in accounts from earlier historic times the disease cannot be recognized with certainty, there is a strong probability that many of the plagues occurring under such circumstances were typhus. Early in the sixteenth century appear the first undoubted descriptions of the disease in Italy and in Spain. From then on each century showed a series of recurring epidemics throughout Europe, most widespread and severe in connection with each of the many wars, up to and including the Crimean and Russo-Turkish Wars of the nineteenth century. Great Britain and Ireland as well as the Continent have been inflicted by a long series of epidemics, and in these countries the disease still smoulders. But as the nineteenth century drew to a close the world saw a general lull in the incidence of typhus epidemics which left it all the more unprepared for the present outbreak. Of late years, before the Great War, the disease has been confined to endemic foci, notably Poland and southwestern Russia, Ireland, Algeria, Mexico, and Manchuria. Mexico, it is to be noted, has been a stronghold of typhus in endemic or epidemic form ever since the entrance of Europeans early in the sixteenth century. In the United States typhus fever has never figured to the extent that it has in Europe; it was, however, prevalent in the first half of the nineteenth century, particularly in connection with the Irish immigration in 1846-7.

Although the clinical picture of typhus fever can be recognized in the descriptions of older writers, typhus was not distinguished from typhoid fever until the work of Louis in 1829. The similarity in the names used for the two diseases is unfortunate, since to this is probably due the persistent impression among the laity, and even among ill-informed physicians, that the two diseases are related. Aside from a superficial similarity, in that both involve continued fever, eruption, and delirium, the two diseases are totally distinct. Typhus fever is much more closely related to Rocky Mountain spotted fever than typhoid.

Our understanding of the disease in its epidemiologic aspects has been greatly illuminated by the demonstration by Nicolle in

1909-10. amply confirmed by subsequent workers, that it is transmitted by the body louse. This fact explains so fully and clearly many features that were previously buried in mystery as to cause wonder that it was not suspected long ago. The fact of louse transmission, moreover, furnishes a sound foundation for effective prophylaxis. In 1920 the authors, with Dr. John L. Todd, were able to demonstrate that the disease is due to infection with *Rickettsia prowazeki* previously described by Ricketts, v. Prowazek, da Rocha-Lima, and others in typhus-infected lice.

Definition.—Typhus fever is an acute febrile disease characterized clinically by an abrupt onset and termination by rapid lysis after a course averaging fourteen days; a macular eruption, tending to become hemorrhagic, general over the body and extremities, but avoiding the face; delirium which may pass into a fatal coma; a tracheobronchitis and a susceptibility to bronchopneumonia. Infection occurs through the bite of a body louse previously infected with *Rickettsia prowazeki* by feeding upon another patient. Pathologically the disease is characterized by lesions of the blood-vessels of the skin, musculature, and central nervous system; in the walls of blood-vessels involved in these lesions minute micro-organisms are found which are believed to be the infecting agent in the human host as are the *Rickettsia prowazeki* in the louse.

Etiology.—Typhus fever has long resisted attempts to demonstrate its specific infectious agent. A series of micro-organisms have been cultivated one after another from patients having typhus fever, and many of these have been proposed by their finders as the cause of the disease. The best opinion among investigators, however, has remained unfavorable to these claims, holding that typhus fever is a disease in which secondary invaders are peculiarly prone to occur and even to produce immunologic reactions.

Ricketts in 1910, Hegler and von Prowazek in 1913, and da Rocha-Lima in 1916 described in typhus-bearing lice certain bacterium-like bodies named by da Rocha-Lima *Rickettsia prowazeki*.

Being impressed by certain analogies between typhus fever and Rocky Mountain spotted fever, one of us (Wolbach) in 1919 visited Mexico, and in 1920 organized the expedition to Poland at the invitation of the League of Red Cross Societies with the object of investigating typhus fever by methods similar to those used by him in the study of Rocky Mountain spotted fever. As a result of the Mexican expedition Wolbach and Todd found organisms consistent with *Rickettsia prowazeki* in the vascular lesions of the skin in Mexican typhus. From the studies instituted in Poland it is proved: First, that lice previously free from *Rickettsia* when fed on patients with typhus fever during the first ten days of the disease in a very high percentage acquired organisms answering to the descriptions of *Rickettsia prowazeki*; second, that organisms consistent with *Rickettsia prowazeki* were found in vascular lesions of the skin of typhus patients, both at autopsy and in specimens excised during life; third, that the presence of *Rickettsia prowazeki* in lice fed upon typhus patients was necessary in the transmission of typhus fever by the method of injecting the intestinal tracts of these lice into animals.

In human tissues the *Rickettsia* occur singly or in clumps in the endothelial cells of blood-vessels. They have the appearance of minute paired ovoid bacteria or bipolar staining rods, smaller than the influenza bacillus, the total length of pairs and rods being in the neighborhood of 1 micron or less. They are most easily demonstrable in pairs 1 to 1.5 long, usually surrounded by an unstained space, either singly or in clumps. Other more minute paired forms are found in larger collections filling endothelial cells. In the louse the organism exhibits a greater range of size and morphology; different forms ranging from bacillary and filamentous forms to exceedingly minute paired coccoid bodies follow in sequence and suggest a definite cycle of development. When the infection in the louse has reached its maximum practically every cell of the epithelium of the gut is enormously distended with myriads of minute organisms. These organisms, like the organism of Rocky Mountain spotted fever, are decolorized by Gram's method and

take ordinary stains with difficulty, requiring one of the Romanowsky stains, preferably Giemsa's modification, for their satisfactory demonstration. Also, like *Derma-centro-xenus rickettsi* of Rocky Mountain spotted fever, they have resisted all attempts at cultivation. From these and other similarities it is possible that the two belong together in a hitherto unknown group.

The transmission of typhus fever by the body or clothes louse, as demonstrated by Nicolle and others, has been mentioned in the introduction. Lice fed upon patients with typhus fever become infective within an interval of six or more days, consistent with the interval required for the development of *Rickettsia*. The infected louse transmits the infection in the act of feeding upon a human host. The disease in man has been produced by a single louse in one feeding. The ability of the head-louse to transmit typhus fever has been proved experimentally, but in spite of this fact the head louse is probably of little importance in transmitting the disease since epidemics seem to occur only with the prevalence of the body or clothing louse, and do not occur in tropical countries where head lice are common, but body lice are rare. The pubic louse, as well as the flea and bedbug, is not connected with the spread of typhus. The possibility of infection by virus contained in the excreta of infected lice entering the body, through scratches or otherwise as well as by the act of feeding, has been discussed. The fact that the virus in excreta is quickly destroyed by drying, however, argues against this as an important source of infection.

The possibility of contracting the disease otherwise than through the louse is improbable. Laboratory monkeys and guinea-pigs can be infected directly from human patients only by rather large intraperitoneal injections of patients' blood. Supposed cases of direct contagion from patients have probably in reality been due to undiscovered bites of lice.

Incidence.—Typhus epidemics tend to reach their maximum in the spring and to subside with the advent of warmer weather. Epidemics, however, may occur at any season. It is probable that the incidence according to season is purely a matter of con-

ditions favoring the prevalence and transference of lice. The same is probably true of variations of incidence between the sexes. All ages are attacked, although the disease, being relatively mild in children, has its chief importance as a disease of adults. In epidemics many or all members of a household may come down with the disease almost simultaneously or in succession.

While prevalence of louse infestation is necessary to the occurrence of an epidemic, it is to be borne in mind that it is not only the louse-infested classes that contract typhus. It is not louse infestation, but the single bite of an infected louse that infects, and probably no person who has not had the disease is immune. Thus any louse-free person who receives a louse from a typhus patient is in danger of contracting typhus, although if this louse is destroyed and no more are received this person will not be a source of infection to others. Thus, when typhus is epidemic, physicians, nurses, orderlies, ambulance drivers, attendants at delousing stations, and all others whose work brings them in contact with typhus cases are in positions of great danger. The mortality among physicians and particularly among military surgeons in recent years in Poland is said to have been very great.

The usual incubation period in man is stated to be from eight to fourteen days.

Pathology.—Autopsies in cases of uncomplicated typhus show no constant gross lesions other than remains of the rash which can be described as characteristic. Microscopically, however, a distinctive pathology exists in specific lesions of the blood-vessels, especially the vessels of the skin and of the central nervous system, corresponding with the seats of the two most striking clinical manifestations of the disease, the eruption and the nervous phenomena. These lesions were first discovered in the skin by Fränkel in 1914. Fränkel's observations have been confirmed and extended by the work of a number of German pathologists as well as by our own series of autopsies. The lesion starts with a proliferation of the endothelium resulting in an accumulation of swollen cells followed by degeneration and

necrosis, then thrombosis, which in smaller vessels often causes complete occlusion. The initial reaction in capillaries frequently causes destruction of continuity of the vessel wall resulting in extravasation of blood as in the petechiæ. In the brain these lesions produce minute areas of necrosis and proliferation. These correspond in size to miliary tubercles and were present in surprising abundance in all of the 39 postmortems of our series, especially in the midbrain, basal ganglia, medulla, and cortex of the cerebrum. While these specific typhus lesions were found most conspicuously in the skin and in the brain, they are by no means confined to these locations, having been encountered, with or without suspected connection with clinical symptoms, in the myocardium, lung, kidney, lymph-nodes, testis, and skeletal muscles. Occasionally large blood-vessels are involved in the typhus lesion with complete thrombosis as a result. In our series the following important thromboses occurred: superior mesenteric with infarction of small intestine; left internal carotid with cerebral softening; a main branch of the left pulmonary artery; main branches of the splenic artery. In instances of gangrene of the skin and subcutaneous tissue the lesion is due to an extensive thrombosis of capillaries, small veins and arteries beginning in the skin and extending centripetally without involvement of large vessels.

Other postmortem findings not distinctive of typhus but noteworthy for their bearings upon the disease picture may be mentioned, as the following: In fatal cases of typhus, bronchitis and bronchopneumonia are almost invariably present. The trachea and bronchi are deeply injected and covered with brownish puriform exudate. Bronchopneumonia of greater or less extent was demonstrable in 37 of our 39 autopsies. The myocardium, though most commonly firm and normal red in color, in 6 of our cases showed pallor and friability due to edema from unusually extensive lesions of the blood-vessels. The spleen in cases dying before the end of the second week is usually enlarged; the consistency is firmer than in typhoid. The bone-marrow from the femur as a rule shows a reaction varying from a red mottling of actively erythrogenic areas in the earlier cases

to completely red marrow in the later cases. The brain and meninges are often deeply injected with sometimes slight edema, but the gross changes are slight in comparison with the histologic findings. The parotid and submaxillary glands are subject to pyogenic infections. The alimentary tract, including the liver and pancreas, the kidneys, the ductless glands, the lymph-nodes, the endocardium, and the serous membranes are rarely the seat of important pathologic processes.

Symptoms.—Typhus fever is a disease with an abrupt onset. On a certain day the patient becomes suddenly seriously ill, and from this day the duration of the disease is to be counted. In qualification of this statement as to the acuteness of the onset it is to be mentioned that there is some reason to suspect the existence of a prodromal stage, since many patients on questioning describe certain vague feelings of malaise, fatigue, weakness, faintness, or nervousness for one, two, or sometimes more days in advance. These possible prodromal symptoms, however, are too vague to be of diagnostic value. The true invasion is not a gradual culmination of these, but an event in itself.

The commonest presenting symptom of the onset is headache, which is usually described as of great severity. A majority of the cases have a chill with onset, and the chill is commonly repeated one or more times during the first two days. Pain in back and limbs was present in half of our cases, but was usually overshadowed by the headache. About a third of our cases vomited with onset. Of our 181 cases, 161 had headache; 134 had a chill, in 84 repeated one or more times; 97 had pain in back and limbs; 53 vomited; 5 had only a general febrile malaise and prostration without other more definite symptoms. In the early days of illness 88 had insomnia; 77 had anorexia; the remainder having no marked disturbance of appetite; 157 were constipated.

From this it will be seen that the symptoms of invasion of typhus while fairly uniform have little except for the tendency to irregularly repeated chills that can be considered as characteristic to distinguish them from those of other acute febrile diseases.

The same is true of the results of examination in the pre-

eruptive stage. The usual picture is that of an obviously feverish patient, uncomfortable and anxious, often already somewhat delirious. The face is apt to be flushed and there may be beginning injection of the conjunctivæ. There may be a slight dry cough, but the general physical examination is negative except for possible enlargement of the spleen.

From the onset until the appearance of the eruption the patient continues as a case of unexplained fever, suspected of typhus or not according to circumstances, but not conclusively proved. In the course of this period the headache commonly diminishes or disappears.

At a time varying from the third to the seventh day the diagnosis is cleared by the appearance of the eruption. This consists at first of discrete pink macules, round, oval or irregular, usually from 2 to 5 mm. in greatest diameter, non-palpable, and disappearing on pressure. They may be first discernible on some special part of the body, perhaps most commonly on the chest, the back, about the shoulders, or at the base of the neck about the clavicles. In other cases they are first seen on the abdomen. on the forearms and lower legs, or on the dorsa of the hands and feet. But almost from the first the lesions of the eruption can be made out distributed in greater or less profusion generally over the trunk and extremities, only avoiding the face. The non-appearance of the eruption on the face is to be emphasized. Among our 181 cases, 6 cases with extremely profuse eruptions general elsewhere had single or a very few lesions on the face, which were noted as curiosities; the remainder, however numerous the lesions on neck, trunk, arms, and legs, had no lesions on the face. Lesions on the palms are also rare. The profusion with which the lesions forming the eruption are distributed is variable, but it is a poor eruption that does not show its elements more thickly distributed than a more than usually profuse eruption of rose spots in typhoid fever. Rarely the lesions are almost confluent, so as to suggest in the early stages, except for the location, the eruption of measles; on close examination, however, the lesions are seen to be more sharply defined and not elevated. Ordinarily the lesions are numerous,

but remain discrete. After the first appearance of the eruption it continues to become more conspicuous by increase in the number and size of its elements and also by changes in color. It first changes from a reddish pink to a brighter red, then in severe cases to a violet purple. This last change is due chiefly to general cyanosis of the patient rather than to extravasation of blood, since while many lesions at this stage on pressure are found to have hemorrhage within them, on pressure or after death the greater part of the purple discoloration disappears. Occasionally a case is found some of whose lesions, though otherwise typical both in appearance and on histologic examination, are distinctly palpable as papules. In a certain proportion (23 of our 181 cases) the true eruption for a few days early in the second week was overlain by a diffuse mottled or blotchy erythema, subsiding before the disappearance of the true eruption. The typical eruption of typhus remains in evidence until the beginning of favorable defervescence, when it disappears rapidly, leaving only slight brownish discolorations; in cases passing into a fatal stupor, to be described later, the rash remains prominent to the end in spite of normal temperatures.

The individual lesions when examined by focusing a microscope of 20 to 40 diameters on their surface, the skin having first been cleared with petrolatum, are seen each to consist of a tangled network of dilated venules.

The stage of eruption has certain characteristics to be noted other than the presence of the rash. With its beginning the headache of onset has usually disappeared, but from this time on one commonly sees an increase in the two chief features of the later course, delirium and bronchitis. It is chiefly upon the course of the second week that the outcome of the case depends.

Of symptoms at the beginning of this stage most patients who are able to specify complain only of general febrile prostration, restlessness, insomnia or disturbed sleep, and cough. On examination many are objectively outspokenly delirious. The delirium may be either of the excited or of the dull variety, but in our cases excitement was nearly twice as common as dulness. The facies is apt to show a tense expression, corresponding with

abnormal mental activity, or relaxation with stupor. The face is commonly flushed, and the conjunctivæ in the great majority of cases are injected, although this injection becomes more constant and intense later. The tongue in all severe cases shows beginning dryness. The throat may or may not show moderate redness of the fauces. Labial herpes is infrequent. Cough is usually present, but not yet troublesome; it is at first dry, but soon becomes loose, with excessive tracheal secretion. The lungs may show diffuse musical râles which tend later to disappear, and may also show crepitant râles at one or both bases which are present in most of the cases in the second week. The

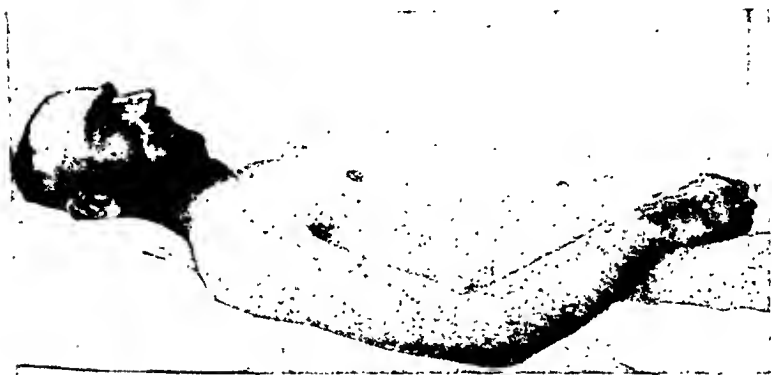


Fig. 223.—A case of typhus fever showing the typical eruption.

heart tends to marked acceleration of rate, but rarely shows organic murmurs. Occasional cases show absolute irregularity. The spleen is often palpable, but rarely extends much beyond the costal margin; it tends to recede as the disease progresses.

White blood counts as reported by Dr. Stella Naparalska on our cases show variations from leukopenia to leukocytosis, but most commonly a slight leukocytosis. Cases with higher leukocytoses showed a higher percentage of mortality, but some cases with high white counts failed to show serious symptoms or complications. The Weil-Felix agglutination reaction is very constantly positive. The urine is concentrated and shows slight to moderate albuminuria and cylindruria as in other fevers.

From the appearance of the eruption onward extends the most serious period of the disease. Uncomplicated cases continue febrile and more or less delirious, particularly at night, but without other special symptoms until about the twelfth day the patient is found to be distinctly better, quieter and more comfortable, less flushed, and with rash distinctly fading. The temperature is lower and continues to fall either by a series of remissions or by a gradual decline, until two or three days later it becomes permanently normal. More cases have a more or less troublesome cough which may be an important factor in their increasing exhaustion. The lungs show numerous crepitant râles at one or both bases or even throughout both lungs; moist râles at one or both bases were found in 144 of our 181 cases. But as the primary symptoms of typhus subside, as shown by falling temperature and receding rash, the general condition improves rapidly, even though the cough may for a time continue. Nearly all severe cases breathe through their mouths, which get extremely dry and fissured in spite of all care, rendering nutrition difficult. Incontinence of urine and feces is common in the delirium, and increases the difficulty of nursing. But the disappearance of all these symptoms as convalescence begins is rapid and satisfactory.

In the early stages of convalescence patients frequently complain of noises in the head, of vertigo, and occasionally of nausea. Many have deafness, apparently of central origin. A large proportion, even including many who were not suspected of delirium, have no memory of events of the febrile period after the onset of the disease. A few show psychic peculiarities for a time. But these symptoms all tend to improve. The return of strength and nutrition to normal after typhus fever is rapid, although the return to normal intellectual vigor may be slow.

Complications.—In our cases the presence of high fever and of symptoms directly referable to high fever did not seem to be the controlling factor in the outcome. Cases with high temperatures showed exhaustion as would be expected in general proportion to the degree of fever, but the self-limitation of the disease

could be counted on to assert itself and bring relief before febrile exhaustion alone proved fatal. Our fatal cases were due mainly to one or both of two special causes, one incident to the disease process of typhus and the other a complication, namely, typhus encephalitis and bronchopneumonia.

The occurrence of microscopic lesions in the brain has been described in the section on Pathology. Clinically in certain cases, not necessarily those that have shown severe symptoms in the earlier stages of their course, but always adults and most commonly patients past middle life, a stupor gradually develops during the second week which persists in spite of normal temperatures until, after a period of increasing emaciation and exhaustion, the patient dies, most commonly from a terminal bronchopneumonia. The condition in this period, which may last for a week or more, is not one of complete coma, since, although the patient cannot be roused to respond to questions and often not even to take nourishment, he frequently groans persistently and noisily, moves his arms restlessly and aimlessly, and picks at the bedclothes. Some show constant violent twitchings and contortions of the facial muscles, and a jerky, slightly spastic tremulousness of other parts of the body. The rash remains evident to the end, even three weeks or more after the onset. The temperature (rectal) is commonly normal or subnormal through this period; the pulse is almost or quite impalpable in the cold and cyanotic extremities; the respiration may be accelerated, but there is no evident dyspnea. Some hours before death, however, there is a terminal rise of temperature and urgent dyspnea appears. In cases dying in this manner the histologic cerebral lesions are found to be exceptionally numerous.

Bronchopneumonia, the most important complication of typhus, is a factor of confusingly variable significance. In some cases it makes its appearance with an immediate change in the whole aspect of the case, converting a case previously ordinary or mild at once into one of unfavorable prognosis. In other instances areas of more or less extensive consolidation of a lung are found in the course of routine examination that resolve in

convalescence without the patient at any time showing symptoms other than those of uncomplicated typhus fever. The onset of bronchopneumonia *with symptoms* is commonly marked by the appearance of rapid labored breathing with acceleration and weakness of the pulse. Some cases fall almost immediately into a state of collapse, after which death is only a matter of hours. Others survive long enough for recognition of local consolidation. It was our experience, however, that of the cases that developed urgent pneumonic dyspnea in the course of typhus fever few recovered; whereas, if consolidation was discovered without previous pneumonic symptoms no further unfavorable influence upon the course of the disease need be apprehended.

Parotitis and infection of the submaxillary glands occur more frequently in typhus than in other fevers, undoubtedly by extension of pyogenic infection from the mouth. It is common for a number of cases to appear simultaneously in one ward, suggesting that the agent of this secondary infection may be carried from one patient to others. One such appearance of several cases at once occurred in our service; after correction of certain imperfections in the system of sterilization of dishes, utensils, and mouth-cleaning instruments no more cases developed. These infections of salivary glands appear usually late in the disease, or even in early convalescence. They manifest themselves by swelling and more or less pain in the gland or glands attacked, but are not accompanied by much increase in fever or marked constitutional symptoms. Nearly all suppurate and require surgical drainage.

Typhus gangrene is a complication which figures with varying prominence in different epidemics. In some epidemics, particularly among soldiers, it attacks the feet and toes of large numbers. In our series it was represented only by the appearance of gangrenous areas over bony prominences in a few cases. In these the first stage was marked by the appearance of an area of moderately deep induration with a distinct slightly elevated margin. With careful relief of pressure one case was arrested at this stage, but the remainder showed in such areas during the next two days a progressive discoloration through a

dull red to a purplish black. In cases that survived, the blackened skin and subcutaneous tissue gradually separated as a malodorous slough and was removed, leaving a deep crater which healed by slow granulation. In one fatal case in a stout patient there was at the time of death a freshly developed area of gangrene over the right hip. On incision, postmortem, the necrosis was found to extend a number of centimeters into the subcutaneous tissue. Typhus gangrene shows a distinct tendency to symmetric bilateral distribution, as in both feet, both buttocks, both elbows, or on one hip and on the opposite knee.

Cases of typhus have been reputed to be subject to cutaneous sepsis, so much so that some have advised avoidance of hypodermic medication. In our service, however, no instance of abscess from a hypodermic occurred, although hypodermic injections were given freely. We had one case of severe phlegmonous sepsis at the ankle, and one case of erysipelas as the terminal event in a patient with persistent cerebral symptoms. Otitis media is not uncommon.

Through the course of typhus the bowels are most commonly constipated. Occasionally, however, a diarrhea appears as an intercurrent event. Retention of urine is not infrequent.

Diagnosis.—In the early days of typhus fever the diagnosis can be made only tentatively from the circumstances of the case and from the suggestiveness of the symptoms of onset. In the presence of an epidemic or after known exposure a patient with these symptoms should be regarded as probably having typhus, while in the absence of other cases the chances of a case with these symptoms having typhus are remote. By the end of the first week, on the other hand, most cases show an eruption that places the diagnosis beyond question. In a few cases diagnosis by the eruption may be impossible. Cases without eruption have been said to occur, though this is doubtful. But the great source of uncertainty is the presence among typhus suspects of other skin lesions that may obscure eruptions that would otherwise be distinct. Many typhus patients when first brought to a hospital are so covered with dirt, flea-bites, pediculosis of long standing, with pigmentations and scratch-marks

new and old, scabies, acne and impetigo, that there is little if any undiseased skin to examine. Such cases have to be judged by their subsequent course.

Of distinct assistance in diagnosis is the Weil-Felix reaction. By the curious discovery of its authors it has been found that the blood of typhus cases has very constantly a power to agglutinate cultures of the organism known as *Bacillus proteus* X-19, cultivated in several strains from the urine of typhus patients, although this organism has nothing to do with the production of typhus fever. So constant is this agglutinating power, often in extremely high dilutions, that some regard the reaction as of value for the diagnosis of typhus as great as that of the Widal reaction for typhoid. Undoubtedly, in clinics where typhus is prevalent diagnoses according to the Weil-Felix reaction are rarely in error. It must still be questioned, however, whether the non-occurrence of this somewhat peculiar reaction among patients in this country is sufficiently proved to warrant our making positive diagnoses of typhus fever on the strength of this reaction alone.

In cases where absolute proof of the presence of typhus fever is required, one of the skin lesions may be excised under local anesthesia for histologic examination.

In differential diagnosis in the early stages a wide range of febrile diseases with sudden onset must be considered. In Poland relapsing fever is perhaps the commonest disease to be distinguished, but is recognized by its less severe constitutional symptoms and by demonstration of spirochetes in the blood, as well as by its recurrences. When influenza and typhus were both epidemic, early differentiation could be made only tentatively from the greater prominence of headache and chills in typhus, and of general pains and of coryza in influenza. Pneumonia, meningitis, malaria, scarlatina, smallpox, and septicemias are to be distinguished chiefly by their own positive characteristics. In these, with the exception of malaria and measles, the leukocytosis is greater than is common in early typhus.

Before the end of the first week the diagnosis in most cases of typhus fever is placed beyond doubt by the appearance of

the eruption. Yet, as has been mentioned above, there are occasional cases in which the eruption is rendered uncertain by the presence of other lesions of the skin. If in such cases there is the additional difficulty that no history of the mode of onset and of the duration of the illness can be obtained, there may be uncertainty in differentiating between typhus and typhoid fevers. Disregarding history and eruptions, the differences between typhus and typhoid patients at the height of their respective diseases may be stated as follows: The typhus patient commonly seems more acutely ill with a more excited type of delirium and rapid pulse; his face is more flushed and his conjunctivæ are injected; cough and cyanosis are more apt to be present. The typhoid patient is more apt to be in a passive somnolent condition, more uniform in his behavior from hour to hour, with slower pulse; he may show more pallor and emaciation, since he may have been ill for a longer period; he is more apt to have an enlarged spleen and abdominal distention, and abnormalities of the stools. The Weil-Felix and the Widal agglutinations and cultivation tests for the typhoid bacillus give valuable assistance in such conditions. The later course of the case also will usually furnish grounds for a decision, since the typhus patient will improve earlier and more rapidly, or die with symptoms of bronchopneumonia or afebrile stupor, whereas the typhoid patient will improve in the course of a slow lysis, the mental condition improving with the fall in temperature, or may die of perforation or hemorrhage.

Cases of typhus fever in terminal stupor may show retraction of the neck and Kernig's sign suggesting meningitis, to be excluded by lumbar puncture.

Prognosis.—The mortality in typhus fever varies widely in different epidemics and perhaps in different peoples and different social classes. Some epidemics are reported to have had mortalities as high as 50 per cent.; others have had mortalities of little over 5 per cent., as was the case with the epidemic in Poland in 1920. We were told that the Germans in Poland in the previous years had had the disease with a larger proportion of deaths than the native Poles. It was also stated with emphasis

by Polish physicians that educated persons, particularly physicians, who contracted typhus were much more apt to die than patients from the lower classes.

The age of the patient is an important factor in the prognosis. On our service, in which were collected cases of more than average severity from the general admissions of the St. Stanislaus Hospital, among 40 cases under twenty years of age there were no deaths; among 122 cases of ages under forty, 6 died, or 4.9 per cent.; among 59 cases of ages over forty, 18 died, or 30.5 per cent. The mortality for each decade of age above twenty showed a progressive increase.

In judging the probable outcome of any individual case it was our experience that the age of the patient was a more important consideration than the severity of the febrile symptoms of the earlier stages of the disease. Younger patients, however high their temperatures, almost invariably survived, whereas older patients, even though at first they might seem to be mild cases, would often suddenly develop bronchopneumonia or gradually pass into stupor. Still at any age there are both mild cases and severe ones, and in general for that age the prognosis is better or worse according to the height of the fever and pulse, the severity of the delirium, and the intensity of the rash. Cases with severe bronchitis are somewhat more subject to bronchopneumonia, but bronchopneumonia may appear in cases in which the bronchitis has been slight. A high leukocytosis increases somewhat the gravity of the prognosis.

Prophylaxis.—The prevention and control of large epidemics involves the general delousing of populations and the isolation as well as delousing of cases, suspects, and contacts. Although compulsory delousing has not been instituted among us except at quarantine stations, and is not imminent, still all who are in positions from which they can influence louse infested classes should make an effort to persuade louse infested persons to free their bodies and clothes of such vermin.

Typhus patients or suspects should be deloused, and the course through which each one of them has moved from before the onset of symptoms until exit from the delousing room is to

be considered a trail of danger. All along this trail are presumably scattered infected lice, a single bite from any one of which will produce typhus in any non-immune person. Places at which such patients have stayed or slept should be quarantined and so treated that no lice can survive in clothes, bedding, furniture, floor, or walls. Other parts of the trail, not forgetting the ambulance, should be dealt with on similar principles. Typhus immunes should be employed so far as is possible in dealing with typhus patients and their surroundings until all lice have been destroyed. All persons who have been in close contact with a typhus patient or suspect should be deloused and kept louse free, in quarantine if possible.

A hospital properly arranged to receive typhus patients should have an admission delousing room with separate entrance and exit, so that the patients can be received from the ambulance at the entrance, louse infested, and later be passed through the exit to the wards louse free. Near the entrance of the delousing room there should be a large steam-sterilizing chamber, so that after the patient has been stripped of all clothing on the stretcher at the entrance and removed to the delousing table the clothes and blankets, still on the stretcher, can be taken back through the door of entrance to the sterilizer.

The delousing room should have also a table with arrangement so that water will drain from it not on to the floor. The patient should be lifted to this table stripped from the stretcher. All body hairs thick enough to conceal lice should be clipped close, with special attention to the pubic and anal regions, since body lice as well as pubic lice may occur in these locations. All clippings should be gathered carefully and either boiled or burned. The whole body except the head should then be bathed thoroughly with soap and hot water, and dried. The head, axillæ, pubic, and anal regions should then be treated with a light oil (kerosene) and the same should be rubbed lightly over the remainder of the body. The head should then be tied up in a cloth; the patient can then be given a night-shirt and be carried to his ward on a clean stretcher. The floor of the delousing room and the table should be gone over with kerosene cloths

and mops after each case. Passing of all persons from the delousing room to the ward should be reduced to a minimum.

Both in the delousing room and in the wards all workers should wear gowns with stocking-footed trousers sewed to the waistband beneath the skirt; and in delousing and other handling of patients rubber gloves should be worn, fitting closely over the wrists of the gown. All should be constantly on the lookout to detect lice, both in the delousing room and in the wards, and physicians in charge should keep close supervision of the delousing process to make sure that it shall always be performed thoroughly.

After each time they are worn gowns should be sterilized by heat or placed with a generous sprinkling of flake naphthalene over each one in air-tight cans for not less than twelve hours.

Treatment.—Typhus fever is a self-limited disease for which no specific process of immunization or therapy has been established. Its treatment, therefore, consists of measures to insure the maximum of rest, comfort, protection, and support to the patient until in due time spontaneous improvement can occur. After delousing, the patient should be made as comfortable as possible in his bed, which should be protected against soiling, and precautions should be taken against his falling out or getting to the windows. Water should be given freely, and a diet of liquids and soft solids at least five times a day, with attention to caloric value. Cups and utensils should be sterilized after use to prevent transfer of secondary infections. The general régime should be much like that customary in typhoid, including care of the mouth, a four-hourly chart with baths according to the temperature readings, and an enema every second day as needed for moving the bowels. While laxatives by mouth are not contraindicated in typhus, in our cases they proved to be strangely ineffectual. Watch should be kept for overdistention of the bladder. For headache ice-bags are useful; antipyretics should be used with caution if at all. Insomnia and slight delirium may be benefited by veronal or its substitutes. For cough preventing sleep codein proved valuable, as well as for exhausting discomfort from any cause. Contrary to some

teachings, we found morphin hypodermically of distinct advantage for such purposes where codein failed. In violent delirium it was our aim to employ physical restraint only to guard against unexpected escapes, and not to limit motion in bed, relying rather on hydrotherapy and sedatives. Hyoscin, hypodermically, either with or without morphin, proved effectual where necessary. The routine use of stimulants, such as digitalis and strychnin, is probably of little value. In critical conditions from bronchopneumonia camphor and caffein may be of benefit. We were unable to use strophanthin as advocated by Danielopolu. In cases passing into stupor nasal or esophageal tube feeding is indicated, but when once the stupor is established there is little hope of the patient's recovery. Danielopolu in such cases reports striking success by injecting 500 c.c. of a solution of chlorin, 0.04 per cent. in normal salt solution, intravenously, twice a day. His report, however, did not reach us in time to enable us to test the method.

In parotitis, ice-bags may diminish the pain and possibly abort the process. Later, poulticing may prepare the way for incision. In threatening gangrene all pressure should be removed from the part involved with the greatest care by appliances adapted to the position. Other complications are to be dealt with as is done in other diseases. In convalescence no treatment is necessary except for protection against too early resumption of mental work.

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Lunt, who was full-time medical supervisor at the school, from the careful family history and past history of the boy as supplied by his parents, and from careful measurements. In addition, x-rays of almost all the boys were made by Dr. George Holmes and the findings taken into consideration. On the basis of this evidence, it was felt that the present material could be divided into normal and abnormal groups more accurately than has usually been possible. Owing to the stress of other duties, Dr. Lunt turned over the necessary data to the writer for analysis. His painstaking notes are gratefully acknowledged.

The weight of these boys (and similarly the height and chest girth) may be considered from two viewpoints:

1. Which of the current standards approaches most nearly to the observed weights of these healthy boys from well-to-do families who are living under ideal health conditions?

2. Judged by the standard just chosen, how many of these school boys are under weight, and how many are fat?

The scarcity of published data on selected subjects such as these and the great importance of further study of them have been discussed by us in a similar report on Groton School boys, and will be amplified in a paper now in preparation regarding children in a country day school (Rivers).

Measurements.—All the observations were made by Dr. Lunt.

Age was recorded to the nearest birthday.

Height, chest girth, and weight were all taken stripped, and to the nearest quarter-inch and nearest pound.

The circumference represents the midpoint between the two values taken at full expansion and forced expiration, exactly at nipple level, arms dependent. The reasons for preferring this *average* to the measurement in the resting (talking) position, and this *level* to the axillary (second costochondral junction) or to the xiphoid level, will be given together with fresh data in the paper on Rivers' School boys.

This perimeter of the thorax affords a quantitative instead of an impressionistic estimate of the types of physique which various observers take into account in interpreting normality.

The subcutaneous layer of fat on the chest unfortunately introduces an error in many cases, and worse than that, a variable error; but at present there seems no satisfactory method of discounting it.

Method of Testing Standards.—This simple procedure has been fully described in a previous paper on adults. In brief, the difference between the actual weight of each person and the weight as predicted for him by the method being tested, was first noted in pounds, then translated to a percentage of the actual weight. This percentage is clearly necessary, since, for example, 14 pounds' divergence from the weight of a person of 200 pounds is only 7 per cent., whereas in a child of 100 pounds the prediction error is serious, namely, 14 per cent.

Then these percentage deviations from the 130 calculated weights were summed and averaged, yielding the mean percentage error for the particular method (weight table or formula) under consideration.

TABLE I
SIZE STANDARD FOR PRIVATE SCHOOL BOYS

Referred to Age at Nearest Birthday.

Based on Averages from 380 Boarding and Country Day School Boys After Exclusion of Those Subnormal on Physical Examination.

Age nearest birthday.	Height, net, in inches.	Chest girth, mean, net, in inches.	Number of boys.
6	45.7	22.9	3
7	48.1	22.8	6
8	52.1	24.8	16
9	55.8	25.3	19
10	56.0	26.2	16
11	56.8	27.0	19
12	59.7	27.6	15
13	60.1	28.5	30
14	62.8	30.0	42
15	66.2	31.7	69
16	68.2	33.7	54
17	68.8	34.3	47
18	70.0	35.2	29
19	70.1	35.8	14
20	(71.5)	(40.5)	(1)

TABLE II
WEIGHT STANDARD FOR PRIVATE SCHOOL BOYS

Referred to Nearest Half-inch of Height.

Based on Averages from 380 Boarding and Country Day School Boys After
Exclusion of Those Substandard to Physical Examination.

Height, net, to nearest $\frac{1}{2}$ inch.	Wt., net, to nearest lb.	Number of boys.	Height, net, to nearest $\frac{1}{2}$ inch.	Wt., net, to nearest lb.	Number of boys.
44.5	40	1	60.	86	11
45.	40	0	60.5	89	5
45.5	42	0	61.	92	11
46.	44	2	61.5	95	6
46.5	44	0	62.	97	12
47.	45	1	62.5	101	4
47.5	45	0	63.	104	6
48.	45	3	63.5	107	4
48.5	47	1	64.	110	9
49.	49	2	64.5	112	2
49.5	52	0	65.	114	18
50.	54	4	65.5	117	13
50.5	56	0	66.	119	15
51.	57	1	66.5	122	11
51.5	58	0	67.	125	11
52.	59	5	67.5	129	14
52.5	61	1	68.	132	16
53.	63	10	68.5	135	11
53.5	65	4	69.	137	16
54.	66	6	69.5	139	12
54.5	68	4	70.	140	12
55.	69	3	70.5	142	14
55.5	71	6	71.	144	15
56.	72	11	71.5	148	8
56.5	75	2	72.	152	7
57.	77	7	72.5	156	4
57.5	79	5	73.	160	3
58.	80	9	73.5	161	2
58.5	82	3	74.	162	1
59.	84	9	74.5	162	2
59.5	85	3	75.	161	1
			75.5	169	1

Standards Studied.—These have been rather thoroughly described in the paper on Groton School boys and need not be repeated except for the new tentative Ideal Tables, which are given

TABLE III

WEIGHT STANDARD FOR PRIVATE SCHOOL BOYS

Referred to Nearest Half-inch Chest Girth.

Based on Averages from 380 Boarding and Country Day School Boys After Exclusion of Those Substandard to Physical Examination.

Chest-girth, net, to nearest $\frac{1}{2}$ in.	Wt., net, to nearest lb.	Number of boys.	Chest girth, net, to nearest $\frac{1}{2}$ in.	Wt., net, to nearest lb.	Number of boys.
21.5	37	1	31.5	116	14
22.	40	0	32.	120	13
22.5	43	3	32.5	123	14
23.	47	4	33.	127	19
23.5	51	1	33.5	130	16
24.	54	13	34.	134	13
24.5	58	3	34.5	138	24
25.	62	11	35.	141	22
25.5	66	8	35.5	145	9
26.	70	12	36.	149	18
26.5	74	7	36.5	153	7
27.	78	16	37.	157	7
27.5	82	16	37.5	161	5
28	86	11	38.	165	1
28.5	90	17	38.5	170	1
29.	94	13	39.	176	1
29.5	98	15	39.5	181	0
30.	103	14	40.	187	1
30.5	107	16	40.5	192	1
31.	112	13			

in Tables I, II, and III. The use of the size table needs no description. In predicting weight the two proposed tables are to be applied simultaneously, reading from Table II the weight-for-height, and from Table III the weight-for-chest, then averaging these two values to obtain the predicted (or average normal) weight.

Results.—Regarding Height.—The error in estimating the height-for-age was:

1. According to Ideal Table, 3.16 per cent.
2. According to Baldwin's Table, 4.21 per cent.

Regarding Chest Girth.—The difference between the calculated and observed chest girths, after conversion from inches into percentage of the observed girth, averaged:

1. For Ideal Table, 3.95 per cent.
2. For Porter's Table, 6.20 per cent.

Regarding Weight.—The relative accuracy of the six standards for estimating normal weight was, giving the best first:

1. Weight for height by Ideal Table combined with weight for chest by Ideal Table, with an average error of 4.21 per cent.

2. Weight for chest by Ideal Table, with an error of 4.99 per cent.

3. Wood's Table of Weight for height, less Bowditch's allowances for clothes varying according to age, error of 6.46 per cent.

4. Wood's Table of Weight for height, corrected to give net weight by subtracting 4 pounds throughout, as advised by Wood; error of 6.47 per cent.

5. Ideal Table of weight for height according to averages by inches of heights, with weights for half-inches interpolated; error of 6.57 per cent.

6. Bornhardt's Formula; error of 6.92 per cent.

Comparing the above order of accuracy with the results found in a similar study on Groton School boys, we find that the first three standards in order are exactly the same in both studies, while the last three standards vary somewhat in order. The consolidated results will be discussed in a separate paper describing the manner of construction of the tentative Ideal Tables, but it may be stated that these tables appear from the evidence at present available, and here shown, to be the most suitable for judging the normality of children of the "higher economic classes" (Faber), whether seen in school or in private office work. It is within this somewhat limited but not unimportant field that their use is here urged.

Distribution of Thin and Fat Boys in This School.—The material in hand may now be regarded from another viewpoint—that of the individual. If the tentative Ideal Table be accepted, for the moment at least, as the best suited to judging this type seen in boarding schools, how do the boys in the present series measure up to the table? How many are too thin? How many are too fat?

This may be roughly shown by tabulating the "percentage errors" in groups, as in Table IV.

For this purpose the better procedure would be to recalculate the difference between the predicted and actual weights, referring the percentage to the predicted weight instead of to the actual weight. The greater accuracy thus obtainable has not seemed worth the labor for our present purposes.

The results are:

1. Only 5 boys, or 4 per cent., of the series were excessively thin.

2. Only 1 boy, or 1 per cent., was too fat.

3. This apparent normality must be regarded as literally too good to be true; because (a) as discussed in a similar paper on Groton boys, these boys figured in the composition of the standard with which they have just been compared. This was unavoidable because, if they had been omitted, the material would have been too small to offer even a tentative standard. (b) Furthermore, these 130 boys represent the remainder after exclusion of the observations on a certain number of boys found clinically abnormal. Such abnormalities are, of course, found in any school which studies its own students. In the present series we have obtained some varieties of abnormality which we believed to have no effect on growth, namely, those in paragraphs 1 to 10 below, whereas we have rejected other abnormalities (paragraphs 11 to 15 below) which we believe to affect growth.

Clinically Abnormal Boys.—It may be of interest to summarize the observations which have seemed to us abnormal. They indicate, what may prove of value in judging any particular boy, which physical deviations besides those so well described by Emerson, may be expected to be accompanied by weight deviations of significance.

Abnormal, but Retained.—1. Old endocarditis (C. C. V. D.) perfectly compensated, even under exercise: 5 boys averaging 3 per cent. (0, 1, 2, 5, 8) over average weight by ideal tables, normal (2, 7, —1, —3, —3) in height, and 2 per cent. (0, 0, —1, —3, —5) over chest. In other words, chronic cardiac valvular disease, when compensated, does not interfere with normal growth.

2. Cyanosis and tachycardia, due to congenital heart, but extremely vigorous: 1 boy 3 per cent. overweight, normal in height for his age, and normal in chest for his age.

3. Neurovascular instability: 2 boys each 3 per cent. overweight; in height normal; and in chest girth one normal and one 3 per cent. under normal.

4. Headache persistent and unexplained: 1 boy 4 per cent. overweight, normal height, and 1 per cent. over chest.

5. Orthostatic albuminuria: 2 boys averaging 6 per cent. (3, 8) overheight, 2 per cent. underheight (7, -3), and 1 per cent. (1, 1) under chest. Not enough cases to discuss the interesting relation of physical type to posture and albuminuria.

6. Large liver and spleen, but blood and rest of physical examination normal: 1 boy 6 per cent. overweight, 2 per cent. under height, and 1 per cent. under chest.

7. Fish-urticaria: 1 boy 8 per cent. overweight, 3 per cent. underheight, and 6 per cent. over chest.

8. Apparently slight and delicate, but active and free from illness or physical defect: 2 boys averaging only 3 per cent. (2, 4) below normal weight, but 8 per cent. (6, 10) below normal height, and 9 per cent. (8, 10) below normal chest. It would be most interesting to make a continued study, by following up the after-histories, of a group of boys of this type, since these two boys parallel the interesting case described by Brown (1920):

The more he ate, the thinner and stronger he became. He played on the baseball team and was apparently in tip-top health. We decided that he was one of the "naturally thin" children we hear about.

9. Cough troublesome, but negative physical and radiographic examination: 1 boy whose weight exactly agreed with the tables, whose height was 4 per cent. above normal, and chest 6 per cent. above normal.

10. Boys whose chest x-rays were positive, but whose histories and physical examinations were normal; that the general average weight was not lowered by these 8 boys is indicated by comparison in our usual way of their weights with the combined ideal tables: only 1 boy substandard (by about 3 per cent.), 1

boy exactly normal, and 6 boys from 1 to 8 per cent., or an average of 4 per cent., above the standard. On comparison of the height for age of these 8 boys with the Ideal Table, the average was 0.5 per cent. (1, 3, 3, 3, —1, —1, —2, —4) subnormal, and similar comparison showed the average chest girth for age to be about 2 per cent. (2, 2, —1, —2, —3, —3, —4, —5) above normal.

Abnormal Enough to Require Rejection.—11. Chest x-ray positive and obviously underweight, though otherwise clinically normal: 3 boys averaging 6 per cent. (2, 4, 12) below standard weight for height and chest, 7 per cent. (—2, 6, 16) below height for age, 4 per cent. (4, 4, 5) below chest girth for age. These facts are considered of special significance, as indicating in particular that boys of this group should be watched strictly, and in general as urging the routine physical measurement of school children.

12. Chest x-ray positive, more or less physical signs, and history of rather frequent illness: 5 boys averaging 8 per cent. (4, 6, 6, 11, 11) underweight, 2 per cent. (—3, —4, —7, 1, 4) overweight, 2 per cent. (—2, —5, —6, 12, 13) below chest.

13. Apparently thin and below par: 4 boys averaging 7 per cent. (0, 7, 10, 12) underweight, 3 per cent. (—1, —4, 6, 10) below height, 5 per cent. (—2, +1, 8, 13) below chest. Here anthropometry is of immediate practical service in distinguishing the perilously frail from the "naturally thin" boys described above in paragraph 8.

14. Apparently too fat, without hypophyseal symptoms or signs: 4 boys averaging 7 per cent. (0, 6, 9, 14) overweight, 3 per cent. (2, 2, 3, 5) underheight, 9 per cent. (—4, —5, —12, —13) over chest.

15. Apparently too fat plus some suggestion of Fröhlich's pituitary syndrome, such as scanty hair on body: 3 boys averaging 11 per cent. (8, 8, 17) above weight, 1 per cent. (1, 1, 2) underheight, 6 per cent. (0, —4, —13) over chest.

TABLE IV
THIN AND FAT BOYS

Difference between predicted weight (PW) and actual weight (W) in percentage of actual weight.		Number of boys.
Thin	PW greater than W by 11 per cent. and over (maximum 17 per cent.)	5
	By 1 to 10 per cent.	48
	PW = W	15
Fat	PW less than W by 1 to 10 per cent.	60
	By 11 per cent. and over (highest 13 per cent.)	1
Total		129

Discussion.—What, now, is the practical use of all these figures?

They show for one thing that judgment of the normality of the weight and size of private school boys may be made more accurately by the new Ideal Tables than with the standards in common use by pediatricians. The rather close rivalry in some instances above by these old standards is due, it must be remembered, to the fact that for this study those standards were chosen which seemed the most suitable. If, however, we take other standards into consideration, we shall find stupendous disagreements. For example, there have recently reached this country (1) the book by Von Pirquet describing the weight-for-sitting-height standard which he devised, and has found so useful in feeding the multitudes of underfed children in Vienna; and (2) the book by Dreyer, of Oxford, giving the results of careful studies of stem-length in relation to weight. Both relate weight not to stature, but to the distance from top of the head to the seat. This relationship is intensely interesting not only for judging weight, but for judging stamina. In this connection Hitchcock (1893) credits Ruschenberger of our army with the following belief:

It seems probable that the length of the cerebrospinal column may be a more valuable element in estimating physical qualifications . . . than total stature. Observation has led me to con-

jecture that, as a rule, men of average height, made up of a long trunk and comparatively short lower extremities, possess greater power to endure with impunity great labor and exposure to vicissitudes of all kinds than men who have comparatively long lower limbs and short trunk.

Studies in adults of the two foreign standards quoted are about to be published; but in children observations which permit the desired comparisons have only recently been collected and are now being analyzed. For the moment, however, the purpose of our argument will be indicated by selecting those cases who by our Ideal Tables are normal, and showing how far they vary from the standards of Von Pirquet and of Dreyer.

There were (in 114 Rivers' School boys) 13 such children whose actual weights were identical with their theoretic weights according to the Ideal Tables. From their observed weights, on the other hand, their weights as predicted by Dreyer's standard diverged on the average by 4 per cent., generally too low; whereas Von Pirquet's theoretic weights for these boys averaged 21 per cent. in error, in every instance too high. According to Dreyer's formula most of these boys were too fat, in the worst case by 9 per cent.; whereas according to von Pirquet's all the boys were too fat by from 12 to 36 per cent.!

Von Pirquet's formula accordingly appears totally useless for American private school boys. Whether Dreyer's formula will prove, on careful analysis of the 114 subjects mentioned, to be in general less or more accurate than the Ideal Tables must be a reserved decision.

Conclusions.—1. For judging the development and nutrition of children of the more fortunate classes of the American population totally new standards are necessary.

2. Such standards are tentatively offered for predicting weight, height, and chest girth.

3. Simple tests of these tables, together with parallel control tests of current standards, are presented.

4. The results seem to justify the recommendation of these Ideal Tables for use when dealing with boys of the upper strata of society.

5. Dreyer's new tables may, when experience shall accumulate, prove superior. Data in hand are now being analyzed. Recommendation is therefore made that anybody doing metabolic or other work requiring maximum accuracy should record the additional measurement of stem-length. The technic follows:

The length (λ) is measured by seating the subject on the floor or on a low table (not a chair) with the back against the wall. Care is taken to see that the sacrum is in contact with the wall, and the legs somewhat drawn up, so that the individual sits fairly upon his ischial tuberosities. Under these conditions the height of the top of the head gives a true measurement of the length of the body, and one which is constant and incapable of variation by the subject. If a chair or other form of seat be employed in taking this measurement the individual can by "sitting low" or "sitting high" produce at will a variation of as much as 3 or more per cent. But, since a subject conscious that he is being measured for height tends naturally to produce a full measurement, it will be found that he intentionally "sits up," straightening the spine, tilting the pelvis forward, and rests on the contracted muscles of the thighs and buttocks instead of on his ischial tuberosities. The apparent length—"sitting height," as it has been termed—is thus increased by between 2 and 3 per cent. above the measurement taken in the manner already described. Accordingly, measurements taken on a seat require to be corrected down appropriately before they can be treated as comparable with the measurements of body length in infants or animals (Walker).

The subject places the *backs* of the fingers upon the platform on which he sits, and, with the fingers pointing backward and the knees flexed, lifts the lower portion of the body gently backward until the lowest bony portion of the os sacrum is in contact with the front of the measuring standard. The back is then straightened until the back of the head comes into contact with the standard. It will be found that different persons require to bend the knees in different degrees in order to achieve this position. The head should be tilted neither up nor down and the eyes should look straight forward (Dreyer).

SIZE AND WEIGHT IN BOARDING-SCHOOL BOYS 1911

TABLE V

ORIGINAL OBSERVATIONS ON NORMAL BOARDING-SCHOOL BOYS

No.	Age at nearest birthday.	Height with- out shoes. Inches.	Chest at nipple, mean. Inches.	Weight, net. Pounds.
1.....	13	55.5	27.3	73
2.....	14	58.5	28.	76
3.....	13	56.	27.5	77
4.....	14	58.5	28.5	80
5.....	13	60.	30.	81
6.....	13	58.	27.5	81
7.....	13	62.5	28.	82
8.....	14	57.	27.5	82
9.....	13	59.	28.	83
10.....	14	61.	28.5	84
11.....	13	59.	29.3	86
12.....	13	59.	29.5	87
13.....	14	60.	29.3	88
14.....	15	62.	28.5	90
15.....	15	60.	29.3	90
16.....	13	59.	29.5	90
17.....	14	61.	28.5	90
18.....	14	61.	29.5	91
19.....	13	58.5	28.3	92
20.....	14	63.	29.3	94
21.....	14	65.5	29.5	94
22.....	12	62.	29.3	94
23.....	14	64.	29.	94
24.....	13	62.	28.5	95
25.....	15	61.	30.	98
26.....	14	62.5	29.5	98
27.....	13	60.5	30.8	101
28.....	13	62.5	30.	102
29.....	15	62.	31.5	104
30.....	14	61.	30.	105
31.....	14	62.	31.5	107
32.....	17	66.	31.5	107
33.....	16	68.	30.5	108
34.....	16	65.5	30.5	112
35.....	15	67.5	30.5	112
36.....	14	63.	30.5	112
37.....	14	65.	30.8	113
38.....	16	64.	32.8	113
39.....	17	67.	32	114
40.....	15	64.5	31.5	114
41.....	15	65.5	31.5	114
42.....	16	67.5	32.3	117
43.....	15	64.	32.	119

ORIGINAL OBSERVATIONS ON NORMAL BOARDING-SCHOOL BOYS—*Continued*

No.	Age at nearest birthday.	Height with- out shoes. Inches.	Chest at nipple, mean. Inches.	Weight, net, Pounds.
44.....	15	68.	30.5	119
45.....	17	65.	32.	120
46.....	18	65.	33.	121
47.....	15	65.5	33.	121
48.....	15	65.	31.5	122
49.....	17	67.	31.5	123
50.....	18	65.	33.	123
51.....	16	64.	34.	124
52.....	15	67.5	32.	126
53.....	16	66.5	34.5	126
54.....	17	67.5	33.5	126
55.....	15	67.5	33.	126
56.....	15	70.	34.	126
57.....	15	65.5	32.5	126
58.....	15	68.5	35.3	127
59.....	16	66.3	33.5	127
60.....	17	67.5	33.	127
61.....	15	68.	33.5	128
62.....	17	66.5	34.5	128
63.....	15	68.5	32.5	129
64.....	16	69.	35.	130
65.....	17	69.	33.3	130
66.....	14	67.	34.5	131
67.....	15	66.5	33.3	132
68.....	16	66.	33.	132
69.....	18	72.	33.5	132
70.....	19	66.5	34.5	132
71.....	18	71.5	34.3	133
72.....	17	68.	33.	133
73.....	18	65.5	35.	133
74.....	15	66.	33.	134
75.....	15	68	33.	134
76.....	17	70.5	34.5	134
77.....	16	68.5	34.5	135
78.....	18	67.	34.	135
79.....	18	70.5	35.	135
80.....	15	65.	35.	136
81.....	17	69.5	33.5	137
82.....	18	71.	33.8	137
83.....	17	69.	34.3	138
84.....	16	70	34.5	138
85.....	18	67.	35.8	138
86.....	17	67.	34.3	138
87.....	17	69.	33.	138
88.....	18	71.	36.3	139

SIZE AND WEIGHT IN BOARDING-SCHOOL BOYS 1913

ORIGINAL OBSERVATIONS ON NORMAL BOARDING-SCHOOL BOYS—*Continued*

No.	Age at nearest birthday.	Height without shoes. Inches.	Chest at nipple, mean. Inches.	Weight, net. Pounds.
89.....	19	69.	35.	139
90.....	17	70.5	33.5	139
91.....	19	71.	35.	140
92.....	18	69.	35.5	140
93.....	17	68.5	34.3	141
94.....	15	69.3	33.3	142
95.....	15	67.5	34.3	142
96.....	16	68.5	34.3	143
97.....	16	69.5	35.	143
98.....	16	69.	34.8	143
99.....	19	68.5	35.8	144
100.....	17	68.5	34.8	144
101.....	18	69.5	34.3	145
102.....	15	70.	34.3	146
103.....	17	70.	33.5	147
104.....	16	71.	35.8	147
105.....	17	66.	36.5	147
106.....	17	68.	35.8	147
107.....	18	70.3	35.3	148
108.....	19	72.5	34.8	148
109.....	16	72.	34.3	150
110.....	19	70.5	36.	150
111.....	19	71.	35.8	151
112.....	18	75.	35.5	152
113.....	16	70.3	35.	153
114.....	17	72.	36.3	153
115.....	17	71.	35.5	153
116.....	19	68.	36	154
117.....	16	71.	34.8	155
118.....	16	70.5	35.8	158
119.....	18	69.5	37	159
120.....	16	71.	36.3	159
121.....	18	74.	35.	159
122.....	18	70.	37.5	159
123.....	18	71.	37.	161
124.....	19	73	35.	165
125.....	18	70.	35.8	167
126.....	18	75.5	37.	169
127.....	18	73.5	37.5	170
128.....	19	72	40	172
129.....	15	74.5	37.3	178
130.....	20	71.5	40 5	183

This is practicable in any school, to judge by the extensive experience of Porter (1893):

The larger part of the measurements were made by the teachers, whose hearty co-operation and efficient service in this work should earn them the gratitude of every friend of science.

We are indebted for the opportunity to make this study to the founder and present headmaster of the school, Mr. Frederick Winsor.

The original observations seem worth recording, in view of the paucity of similar data, and are therefore shown in Table V.

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INDEX TO VOLUME 4

- ABDOMEN**, acute, in children, vomiting in, *Sept.*, 441
 routine examination, *Jan.*, 1200
Abdominal angina, *July*, 297
 diagnosis, *July*, 298
 prognosis, *July*, 298
 treatment, *July*, 298
 reflex, *Nov.*, 714
 symptoms of myocardial insufficiency, *July*, 289
Abscess of lung, localized pyopneumothorax and, differentiation, *July*, 98
 subdiaphragmatic, *Jan.*, 1063, 1065
 elevation of diaphragm in, *Jan.*, 1063
Acidosis, *Sept.*, 644
 causes of, *July*, 348
 clinical significance, *July*, 345
 presence and degree of, methods for determining, *July*, 354
 treatment of, *July*, 355; *Sept.*, 645
Acromegaly, *March*, 1465
 with supervening dyspituitarism, case illustrating, *March*, 1469
Acupuncture in lumbago, *Jan.*, 977
Addis and Wilbur's method of estimating urobilin and urobilinogen, *July*, 287
Addison's anemia, *Jan.*, 1239
 disease, *Jan.*, 1255
 case illustrating, *Jan.*, 1228, 1255
 symptoms, *Jan.*, 1255
 treatment, *Jan.*, 1263
Adherent pericardium, *Nov.*, 835
 operative treatment, *Nov.*, 852
Adhesive pericarditis, chronic, etiology of, *Nov.*, 851
 operative treatment, *Nov.*, 852
 pleuritis, high position of diaphragm as result of, *Jan.*, 1060
Adiposis dolorosa, *Jan.*, 1149
 generalized diffuse form, *Jan.*, 1150
 localized diffuse form, *Jan.*, 1150
 nodular form, *Jan.*, 1150
 pathology, *Jan.*, 1151
 treatment, *Jan.*, 1152
Adiposogenitalis, *March*, 1465
Adolescent epilepsy, relation of pituitary to, *March*, 1464
Adrenal asthenia, *March*, 1443
 function, *July*, 60
 line, white, *Jan.*, 1230
Adrenalasthenia, *March*, 1442
Adrenalin, *July*, 61
Adrenals, *July*, 61
 deficiency of, basal metabolic rate in, *Nov.*, 782
Adrenotrope with gastric symptoms, case illustrating, *March*, 1462
Agrostis alba as cause of hay-fever, *May*, 1678
Air-hunger, *March*, 1582
Albuminuria associated with diabetes, *July*, 177
 orthostatic, diagnosis of, *March*, 1599
 etiology of, *March*, 1596
 prognosis of, *March*, 1600
 spinal brace in treatment, *March*, 1595, 1602
 symptoms of, *March*, 1598
 treatment of, *March*, 1600
Alcoholic cirrhosis, definition, *Sept.*, 556
 frequency of jaundice and ascites in, *Sept.*, 559
 symptoms, *Sept.*, 559
Alcoholism, some manifestations, *Jan.*, 1283
Aleukemic myelosis, acute, case illustrating, *March*, 1615, 1623
 chronic, case illustrating, *March*, 1620
Ambrosia artemisiifolia as cause of hay-fever, *May*, 1678
 trifida as cause of hay-fever, *May*, 1680
Amenorrhea, endocrine, *Nov.*, 665
 diagnosis of, *Nov.*, 679
 hormonic signs, *Nov.*, 683
 symptoms of, *Nov.*, 689
 treatment of, *Nov.*, 690
Amitotic myeloblasts, *March*, 1613
Anæmia infantum pseudoleukæmica, *Jan.*, 1132

- Analgesia, *Nov.*, 700
- Anaphylaxis, food, diet in eczema from, *July*, 304
- Anasarca, relief of, in advanced heart failure, *July*, 137
- Anemia, acute aplastic, retinal hemorrhage in, *Jan.*, 1098
- Addison's, *Jan.*, 1239
- aplastic, in early life, *Jan.*, 1132
- curable cases, *May*, 1733
- idiopathic, *Jan.*, 1239
- in early life, *Jan.*, 1125
- treatment, *Jan.*, 1137
- myxedema with, *May*, 1733, 1743
- pernicious, *Jan.*, 1017, 1239
- basal metabolism in, *March*, 1412
- etiology of, *Jan.*, 1240
- gastro-intestinal symptoms, *Jan.*, 1239
- in early life, *Jan.*, 1131
- treatment, *Jan.*, 1138
- of pregnancy, *May*, 1733
- prognosis of, *Jan.*, 1252
- retinal hemorrhage in, *Jan.*, 1097
- spinal cord symptoms, *Jan.*, 1239
- symptoms of, *Jan.*, 1239
- treatment of, *Jan.*, 1024, 1253
- primary, in early life, *Jan.*, 1130
- splenicmegaly with, in early life, *Jan.*, 1136
- pseudoleukemic, in early life, *Jan.*, 1132
- cause, *Jan.*, 1133
- symptoms, *Jan.*, 1134
- treatment, *Jan.*, 1138
- secondary aplastic, retinal hemorrhage in, *Jan.*, 1098
- in early life, *Jan.*, 1127
- causes, *Jan.*, 1127
- symptoms, *Jan.*, 1129
- types of, in early life, *Jan.*, 1125
- varieties of, in early life, *Jan.*, 1125
- Anesthesia, *Nov.*, 700
- Aneurysm of descending aorta, *Sept.*, 459
- diagnosis, *Sept.*, 462
- etiology, *Sept.*, 460
- treatment, *Sept.*, 470
- of thoracic aorta, *Jan.*, 1083
- cases illustrating, *Jan.*, 1084-1090
- Angina, abdominal, *July*, 297; *March*, 1492
- diagnosis of, *July*, 298
- prognosis of, *July*, 298
- treatment of, *July*, 298
- false, *March*, 1492
- minor, *March*, 1492
- mock, *March*, 1492
- pectoris, *March*, 1491
- Angina pectoris, treatment, *March*, 1504
- sine dolore, *March*, 1492
- tobacco, *March*, 1501
- Angle, rectosigmoid, *Nov.*, 901
- subcostal, costal margins, movements of, *Jan.*, 1050
- Angor abdominus, *July*, 297
- Antihemolysin, *March*, 1512
- Antipneumococcus serum in lobar pneumonia, *July*, 191
- in streptococcus pneumonia, *July*, 204
- Antithrombin, *Jan.*, 1006
- Aorta, descending, aneurysm of, *Sept.*, 459
- diagnosis, *Sept.*, 462
- etiology, *Sept.*, 460
- treatment, *Sept.*, 470
- thoracic, aneurysm of, *Jan.*, 1083
- cases illustrating, *Jan.*, 1084-1090
- Aortic disease, pain in, *March*, 1499
- insufficiency, case illustrating, *March*, 1317
- Aortitis with attacks of auricular fibrillation, *July*, 325
- Aplastic anemia, acute, retinal hemorrhage in, *Jan.*, 1098
- in early life, *Jan.*, 1132
- secondary, retinal hemorrhage in, *Jan.*, 1098
- Appendicitis, acute, diagnosis, early, suggestions regarding, *Sept.*, 449
- symptoms of, *Sept.*, 452
- Arborization block, *March*, 1323; *July*, 298
- Arrhythmia, case illustrating, *March*, 1323
- extrasystolic, *Jan.*, 1220
- mixed, *Jan.*, 1224
- perpetual, *May*, 1710
- sinus, *Jan.*, 1219
- Arsphenamin, jaundice following administration, *March*, 1293
- cases illustrating, *March*, 1293-1303
- Arteries, coronary, disease of, *March*, 1491
- pain in, *March*, 1498
- physical signs, *March*, 1502
- Arteriosclerosis, retinal hemorrhage in, *Jan.*, 1095
- Arthritis, chronic, with lamblasis, duodenal biliary drainage in, *Jan.*, 1153
- complicating scarlatina, *March*, 1566, 1568
- focal infection and, *Nov.*, 655

Aseptic fevers, *Nov.*, 750
 Asphyxia as cause of cyanosis in new-born, *Sept.*, 596
 Aspiration, exploratory, of chest, in encapsulated pleural effusions, *July*, 72
 Asthenia, adrenal, *March*, 1443
 neurocirculatory, *March*, 1522; *Nov.*, 754
 variability of blood-pressure in, *July*, 257
 neurosis in, *March*, 1544
 Asthma, bacterial, *May*, 1751
 emphysema associated with, *May*, 1753, 1754
 perennial, *May*, 1751
 pollen, *May*, 1753
 relation of sputum bacteria to, *May*, 1758
 vaccine treatment, *May*, 1751
 Atelectasis, congenital, *Sept.*, 595
 prognosis of, *Sept.*, 598
 treatment of, *Sept.*, 598
 Atherosclerosis, presclerotic stage, *July*, 296
 Atony of rectosigmoid, *Nov.*, 907
 Auricular fibrillation, *July*, 307; *Jan.*, 1221; *May*, 1910
 aortitis with attacks of, *July*, 325
 case illustrating, *March*, 1317
 clinical diagnosis, *July*, 307
 digitalis in, *Nov.*, 885; *May*, 1711
 discussion, description, and tabulation of various types, *July*, 314
 from fright, *July*, 331
 physical signs, *July*, 307
 transient, *July*, 330
 due to coffee, *July*, 330
 with hypertension, *July*, 333
 treatment, *July*, 307; *May*, 1711
 varieties and manifestations, *July*, 307
 flutter, *Jan.*, 1219, 1221
 digitalis in, *Nov.*, 885
 tachycardia, paroxysmal, *May*, 1708, 1710
 Auscultation in diagnosis of mitral stenosis, *Sept.*, 389
 Azotemia, *July*, 13

 BABINSKI reflex, *Nov.*, 713
 Back, lower, pain in, *Jan.*, 973
 treatment, *Jan.*, 987
 Bacteria, sputum, relation of, to asthma, *May*, 1758
 Bacterial asthma, *May*, 1751
 Banti's disease in early life, *Jan.*, 1136
 treatment, *Jan.*, 1139

Basal metabolic rate in deficiency of adrenals, *Nov.*, 782
 of gonads, *Nov.*, 781
 in endocrine disturbance, *Nov.*, 775
 in pituitarism, *Nov.*, 777
 in pluriglandular syndromes, *Nov.*, 782
 in thyroidism, *Nov.*, 775
 metabolism, clinical value, *March*, 1403
 determination, *March*, 1403
 limitations of, in diagnosis, *March*, 1483
 with Benedict portable respiration apparatus, *March*, 1404
 in diabetes mellitus, *March*, 1410
 in disease, *March*, 1408
 in diseases of thyroid gland, *March*, 1415
 in heart disease, *March*, 1411
 in hyperthyroidism, *Jan.*, 1001; *March*, 1415
 in leukemia, *March*, 1412
 in nephritis, *March*, 1411
 in obesity, *March*, 1409
 in pernicious anemia, *March*, 1412
 in tuberculosis, *March*, 1414
 in typhoid fever, *March*, 1413
 value of, *Jan.*, 989
 Belching, *March*, 1592
 Benedict portable respiration apparatus, determination of basal metabolism with, *March*, 1404
 Bilateral lobar pneumonia, *Sept.*, 575
 Bilious attack, *March*, 1590, 1591
 Bilirubin, *July*, 286, 287
 Bladder, stuttering, *Sept.*, 640
 Block, arborization, *March*, 1323
 buffer substances, *July*, 347
 changes in subacute and chronic non-tuberculous pulmonary infections, *Nov.*, 825
 convalescent, in scarlatina, *March*, 1559
 leukemic, oxidase reaction of cells in, *March*, 1614
 normal, leukocytes of, *March*, 1609
 routine examination, *Jan.*, 1202
 tampon substances, *July*, 347
 tests for examination of stomach, *Sept.*, 500
 transfusion, practical aspects, *March*, 1509
 urea nitrogen determination, *Sept.*, 516
 Blood-clotting, Howell's theory, *Jan.*, 1006
 Morawitz's theory, *Jan.*, 1005, 1006

- Circulatory disturbances of pregnancy, *July*, 179
- Cirrhosis, alcoholic, definition of, *Sept.*, 556
- frequency of jaundice and ascites in, *Sept.*, 559
- symptoms, *Sept.*, 559
- of liver, classification, *Sept.*, 555
- factors influencing production of symptoms in, *Sept.*, 557, 559
- of unknown etiology, *Sept.*, 564
- showing jaundice and ascites, *Sept.*, 555
- observations on frequency of symptoms and signs, *Sept.*, 561
- time of appearance, *Sept.*, 559
- syphilitic, *Sept.*, 556
- symptoms of, *Sept.*, 565
- Climacterium, *July*, 67
- and puberty, *July*, 59
- Clinic, medical-social, *Sept.*, 371
- Clinical medicine, routine procedures in, *Jan.*, 1173
- Coffee, transient auricular fibrillation due to, *July*, 330
- Colechicum in gout, *Jan.*, 1043
- Collapse, massive, of lung, diaphragm in, *Jan.*, 1062
- Colon, iliac, spasm of, *Nov.*, 904
- Complemental breast feeding, *Nov.*, 729
- Compression methods for determination of venous pressure, *July*, 240
- Concato's disease, *Nov.*, 849; *March*, 1333
- Congenital atelectasis, *Sept.*, 595
- prognosis, *Sept.*, 598
- treatment, *Sept.*, 598
- heart disease in phthisis, *March*, 1550
- jaundice, *March*, 1305
- Constipation and eczema in an infant from an excess of fat in modified milk, *Sept.*, 585
- chronic, clinical types, *Nov.*, 901
- treatment of, *Nov.*, 902
- simple, uncomplicated, *Nov.*, 902
- Contractures, rectal, *Nov.*, 904
- Convalescence, management of, in lobar pneumonia, *March*, 1423
- Corn as cause of hay-fever, *May*, 1677
- Coronary arteries, disease of, *March*, 1491
- pain in, *March*, 1498
- physical signs, *March*, 1502
- Corpora lutea, *Nov.*, 691
- Corpus luteum, *Nov.*, 691
- Costal margins of subcostal angle, movement, *Jan.*, 1050
- Cough in subacute and chronic nontuberculous pulmonary infections, *Nov.*, 821
- Cranial nerve function, practical points about, *Nov.*, 707
- Creatinuria in hyperthyroidism, *March*, 1401
- Cremasteric reflex, *Nov.*, 714
- Curschmann, ice liver of, *Nov.*, 849
- Cyanosis in newborn, causes, *Sept.*, 596
- Cyclic vomiting in children, *Sept.*, 443
- DACTYLIS glomerata as cause of hay-fever, *May*, 1677
- De Mussy's buttons, *Jan.*, 1056
- Decerebrate rigidity, *Sept.*, 431
- Degeneration, Zenker's, in influenza, *July*, 52
- Delirium cordis, *May*, 1710
- Dementia, postmeningitic, *Nov.*, 919
- præcox, *Nov.*, 926
- Dercum's disease, *Jan.*, 1149
- Dermacentroxenus rickettsi, *May*, 1881
- Desquamation in scarlatina, *March*, 1557, 1558
- Diabetes, albuminuria associated with, *July*, 177
- critical period of hypoglycemia in undernutrition in, *May*, 1728
- dangers of fat in diet, *May*, 1725
- glycosuria associated with, case illustrating, *March*, 1576
- mellitus, basal metabolism in, *March*, 1410
- dysbasia angiosclerotica in, *July*, 237
- gangrene in, *July*, 234
- herpes zoster in, *July*, 237
- neuralgic pains in, *July*, 234
- neurologic causes, *July*, 209
- treatment, *July*, 238
- conditions due primarily to, *July*, 226
- not due primarily to, *July*, 236
- of doubtful origin in, *July*, 237
- effects, *July*, 226
- treatment, *July*, 238
- polyneuritis in, *July*, 236, 237
- reflexes in, *July*, 226
- ulcerations in, *July*, 234
- use of 5 per cent. vegetables in, *Nov.*, 865
- pliability of diet in, *May*, 1723
- practical lessons for physicians and patients in, *May*, 1723

- Diabetes, pseudotabes, *July*, 231
 Diabetic kidney, *July*, 177
 Diagnosis, case for, *Sept.*, 643
 Diaphragm, anatomic considerations, *Jan.*, 1046
 and lung, effusions encapsulated between, diagnosis, *July*, 90
 clinical methods for examination, *Jan.*, 1049
 conditions in which involved, *Jan.*, 1055
 elevation of, in subdiaphragmatic abscess, *Jan.*, 1063
 eventration of, *Jan.*, 1058
 high position, as result of adhesive pleuritis and pulmonary fibrosis, *Jan.*, 1060
 with lessened motility, *Jan.*, 1058
 in massive collapse of lung, *Jan.*, 1062
 in paralysis of phrenic nerve, *Jan.*, 1067
 inspection of, *Jan.*, 1049
 low position, from emphysema, *Jan.*, 1070
 from pericardial effusion, *Jan.*, 1070
 from pleural effusion, *Jan.*, 1068
 from spasm, *Jan.*, 1073
 with lessened motility, causes, *Jan.*, 1068
 palpation of, *Jan.*, 1050
 paralysis of, *Jan.*, 1067
 percussion of, *Jan.*, 1053
 physiologic considerations, *Jan.*, 1046
 sign of Litten, *Jan.*, 1049
 spasm of, *Jan.*, 1073
 x-rays in examination, *Jan.*, 1054
 Diaphragmatic effusions, diagnosis, *July*, 91
 hernia, *Jan.*, 1074
 diagnosis, *Jan.*, 1074
 pleurisy, acute, *Jan.*, 1056
 Diaphragmitis, acute, *Jan.*, 1077
 chronic, *Jan.*, 1077
 Diarrhea, fermentative, *Nov.*, 739
 infantile, *Nov.*, 737
 enteritis and, differentiation, *Nov.*, 737
 severe, *Nov.*, 717
 treatment of, *Nov.*, 722
 treatment of, *Nov.*, 744
 summer, *Nov.*, 737
 Diathesis, hemorrhagic, due to nephritis, *Jan.*, 1096
 Diet in advanced heart failure, *July*, 127
 in eczema, *July*, 301
 due to uric acid retention, *July*, 302
 from food anaphylaxis, *July*, 304
 when nitrogen retention exists, *July*, 303
 in functional gastro-intestinal disturbances, *May*, 1701
 Karell, in advanced heart failure, *July*, 137
 pliability of, in diabetes, *May*, 1723
 salt-free, in advanced heart failure, *July*, 138
 Digestive disorders, functional, management of, *March*, 1537
 Digitalis, body-weight method of administering, *July*, 133
 Eggleston method of administering, *July*, 133, 189
 in advanced heart failure, *July*, 132
 in auricular fibrillation, *Nov.*, 885; *May*, 1711
 flutter, *Nov.*, 885
 in heart disease, *Nov.*, 885
 Dilatation de la croissance, *March*, 1598
 Displacement of heart in phthisis, *March*, 1524
 Dissociation of sensation, *Nov.*, 701
 Diuresis, promotion of, in advanced heart failure, *July*, 138
 Diuretics in edema, *May*, 1642
 in retention of nitrogenous substances, *May*, 1653
 in sodium chlorid retention, *May*, 1652
 in uremia, *May*, 1651
 right and wrong uses, *May*, 1639
 Double lobar pneumonia, *Sept.*, 575
 Duodenal biliary drainage in chronic arthritis, with lamblasis, *Jan.*, 1153
 Duodenum, ulcer of, chronic, diagnosis of, *Sept.*, 506
 Dwarf ragweed as cause of hay-fever, *May*, 1679
 Dysbasia angiosclerotica in diabetes, *July*, 237
 Dyschezia, *Nov.*, 907
 Dysfunction, gastric, in cases of internal secretory disturbance, *Jan.*, 1227
 Dyspituitarism, *March*, 1466
 hereditary, cases illustrating, *March*, 1476
 supervening, acromegaly with, case illustrating, *March*, 1469
 Dyspnea, *March*, 1575
 in advanced heart failure, treatment, *July*, 140
 in heart disease, *May*, 1655

- EARS, routine examination, *Jan.*, 1191
- Eczema and constipation in an infant from an excess of fat in modified milk, *Sept.*, 585
- diet in, *July*, 301
- due to uric acid retention, diet in, *July*, 302
- from food anaphylaxis, diet in, *July*, 304
- when nitrogen retention exists, diet in, *July*, 303
- Edema, diuretics in, *May*, 1642
- relief of, in advanced heart failure, *July*, 137
- Effort syndrome, *Nov.*, 754
- Effusions, diaphragmatic, diagnosis of, *July*, 91
- encapsulated pleural, between lung and diaphragm, diagnosis, *July*, 90
- and mediastinum, diagnosis, *July*, 92
- diagnosis, *July*, 69
- fluid and air in association with, *July*, 96
- interlobar, diagnosis of, *July*, 104
- parietal, diagnosis of, *July*, 70
- secondary changes in chest associated with, *July*, 117
- intrapulmonary, diagnosis of, *July*, 91
- parietal, diagnosis of, *July*, 90
- pericardial, low position of diaphragm from, *Jan.*, 1070
- pleural, low position of diaphragm from, *Jan.*, 1068
- Eggleston method of administering digitalis, *July*, 133, 189
- Ehrlich's reagent, *July*, 285
- Electrocardiogram in diagnosis of mitral stenosis, *Sept.*, 395
- clinical significance of changes in form of, *May*, 1839
- Elimination in advanced heart failure, *July*, 131
- Emphysema associated with asthma, *May*, 1753, 1754
- low position of diaphragm from, *Jan.*, 1070
- Emptying time of stomach, *Sept.*, 505
- Empyema complicating pneumonia, *Sept.*, 47
- diagnosis, *Sept.*, 481
- condition of patient, *Sept.*, 482
- exploratory puncture, *Sept.*, 483
- physical signs, *Sept.*, 482
- x-rays, *Sept.*, 483
- Empyema complicating pneumonia, frequency, *Sept.*, 481
- mortality, *Sept.*, 485
- treatment, *Sept.*, 483
- types, *Sept.*, 478
- diagnosis of, *July*, 69
- intrapulmonary, diagnosis of, *July*, 91
- Encapsulated pleural effusions between lung and diaphragm, diagnosis, *July*, 90
- and mediastinum, diagnosis, *July*, 92
- diagnosis, *July*, 69
- fluid and air in association with, *July*, 92
- interlobar, diagnosis, *July*, 104
- parietal, diagnosis of, *July*, 70
- secondary changes in chest associated with, *July*, 117
- Encephalitis, *Sept.*, 543
- diagnosis, *Sept.*, 550
- lethargia after influenza, *July*, 46
- prognosis, *Sept.*, 551
- summary, *Sept.*, 553
- treatment, *Sept.*, 551
- Endarteritis obliterans, *Jan.*, 1013
- Endocarditis, *Nov.*, 813
- cases illustrating, *Nov.*, 813-818
- Endocrinasthenia, *March*, 1442
- Endocrine amenorrhea, *Nov.*, 665
- diagnosis, *Nov.*, 679
- hormonic signs, *Nov.*, 683
- symptoms, *Nov.*, 689
- treatment, *Nov.*, 690
- disturbance, basal metabolic rate in, *Nov.*, 775
- glands, rôle of, in common medical diseases, *March*, 1437
- in pathogenesis of chronic nephrosis, *July*, 169
- study in, *July*, 59
- Enfants herculés, *Jan.*, 1147
- Enteritis, infantile diarrhea and, differentiation, *Nov.*, 737
- Enuresis in child, *Sept.*, 631
- treatment, *Sept.*, 633
- nocturnal, epileptic fits, and backwardness, with dyspituitary markings, case illustrating, *March*, 1479
- relation of pituitary to, *March*, 1464
- Epidural intraspinal tumor, case illustrating, *May*, 1799
- Epilepsy, adolescent, relation of pituitary to, *March*, 1464
- Epileptic attacks with pituitary markings, case illustrating, *March*, 1481

- Epileptic fits, nocturnal enuresis, and backwardness, with dyspituitary markings, case illustrating, *March*, 1479
- Esophagus, carcinoma of, *Jan.*, 1265
analysis of data on 29 cases, *Jan.*, 1279
cases illustrating, *Jan.*, 1265-1277
pulmonary complications, *Jan.*, 1265
- Essential hypertension, *July*, 27, 296
- Eunuchoidism, *Jan.*, 1143
- Eventration of diaphragm, *Jan.*, 1058
- Ewald test breakfast in examination of stomach, *Sept.*, 497
- Exercise, effects of, on blood-pressure, *July*, 257, 270
in diagnosis of mitral stenosis, *Sept.*, 389
- Exophthalmic goiter, case illustrating, *Jan.*, 1230
- Extra-ocular muscle imbalance, influence of, on general health, *July*, 337
prevalence of, *July*, 337
- Extrasystolic arrhythmia, *Jan.*, 1220
- Eyes, routine examination, *Jan.*, 1191
- FAHR and Vollhard's classification of nephritis, *July*, 15
- False angina, *March*, 1492
- Fat, dangers of, in diabetic diet, *May*, 1725
- Fattening cures, *March*, 1547
- Feeding, breast, complemental, *Nov.*, 729
supplemental, *Nov.*, 734
- Felix-Weil reaction in typhus fever, *May*, 1892
- Fermentative diarrhea, *Nov.*, 739
- Fever, *Nov.*, 747
aseptic, *Nov.*, 750
chemical, *Nov.*, 749
classification of, *Nov.*, 751
high, *Nov.*, 751
hysterical, *Nov.*, 750
in infections, *Nov.*, 747
in neurasthenia, *Nov.*, 753
moderate, *Nov.*, 751
protein metabolism in, *Nov.*, 748
relation of nervous system to, *Nov.*, 750
slight, *Nov.*, 751
subfebrile, *Nov.*, 751
subnormal, *Nov.*, 751
very high, *Nov.*, 751
- Fibrillation, auricular, *July*, 307; *May*, 1710. See also *Auricular fibrillation*.
- Fibrosis, pulmonary, high position of diaphragm as result of, *Jan.*, 1060
- Flint thrill, *Jan.*, 1197
- Flutter, auricular, *Jan.*, 1219, 1221
digitalis in, *Nov.*, 885
- Focal infection and arthritis, *Nov.*, 655
- Food anaphylaxis, diet in eczema from, *July*, 304
- Forme fruste of thyroid deficiency, case illustrating, *March*, 1454
- Fright, auricular fibrillation from, *July*, 331
- Fröhlich's disease, *March*, 1465
syndrome with epileptic fits and nocturnal enuresis, case illustrating, *March*, 1472
- Frontal lobe tumor, *Nov.*, 921
- Functional activity of heart, *March*, 1313
digestive disorders, management, *March*, 1537
gastro-intestinal disturbances, drugs and diets in, *May*, 1701
fatigue group, *May*, 1694
habit group, *May*, 1698
suggestible group, *May*, 1696
treatment, *May*, 1693, 1701
- Fürbringer's sign, *Jan.*, 1065
- GAITS, abnormal, *Nov.*, 702
normal, *Nov.*, 702
- Gangrene complicating typhus fever, *May*, 1890
in diabetes, *July*, 234
- Gärtner's method of determining venous pressure, *July*, 243
- Gastric dysfunction in cases of internal secretory disturbance, *Jan.*, 1227
neuroses, relation of thyro-adrenal apparatus in, *March*, 1440
symptoms in cerebrospinal syphilis, *Jan.*, 1117-1123
- Gastro-intestinal disturbances, functional drugs and diets in, *May*, 1701
fatigue group, *May*, 1694
habit group, *May*, 1698
suggestible group, *May*, 1696
treatment of, *May*, 1693, 1701
symptoms, significance, *March*, 1585
- Gaucher's disease in early life, *Jan.*, 1136
- Genito-adrenal syndrome, *March*, 1367
- Gibson rule, *Jan.*, 1005
- Glandular fever, *July*, 361
bacteriology, *July*, 365
cases illustrating, *July*, 367-370
clinical picture, *July*, 361

- Glandular fever, complications, *July*, 364
 etiology, *July*, 365
 history, *July*, 361
 pathology, *July*, 365
 prognosis, *July*, 367
 treatment, *July*, 367
- Glass capsules for testing _venous pressure, *July*, 240
- Glycosuria associated with diabetes, case illustrating, *March*, 1376
 cases illustrating, *March*, 1376
 renal, *March*, 1375, 1388; *May*, 1731
 significance of, *March*, 1375
- Goetsch test, *Jan.*, 1232
- Goiter, exophthalmic, case illustrating, *Jan.*, 1230
- Gonads, deficiency of, basal metabolic rate in, *Nov.*, 781
- Gordon reflex, *Nov.*, 713
- Gout, colchicum in, *Jan.*, 1043
 tophaceous, *Jan.*, 1029
 treatment, *Jan.*, 1043
 tuberculosis and, relation, *Jan.*, 1042
- Gouty kidney, *Jan.*, 1043
- Graham Steell murmur in mitral stenosis, *Sept.*, 391, 392, 393, 398
- Graves' disease, case illustrating, *Jan.*, 1230
- Growth hypertrophy, *March*, 1598
- HABIT vomiting in children, *Sept.*, 444
- Habitus enteropticus, *March*, 1544
- Hay-fever, seasonal, causes of, *May*, 1673
 treatment of, *May*, 1673
- Heart action, partially irregular, *Jan.*, 1219
 rapid, *May*, 1707
 cases illustrating, *May*, 1712-1721
 totally irregular, *Jan.*, 1222
- disease, acquired, in childhood, *Sept.*, 607
 prognosis, *Sept.*, 609, 615
 treatment, *Sept.*, 609, 615
 basal metabolism in, *March*, 1411
 classification, *March*, 1313, 1314
 congenital, as cause of cyanosis in newborn, *Sept.*, 596
 in phthisis, *March*, 1530
 definition, *Nov.*, 877
 diagnosis, errors in, *Nov.*, 877
 digitalis in, *Nov.*, 885
 dyspnea in, *May*, 1655
 errors in diagnosis, *Nov.*, 877
 in treatment, *Nov.*, 877
 functional capacity of heart in, *Nov.*, 879
- Heart disease, occupational therapy in, *Nov.*, 887
 pulmonary thrombosis in, *Jan.*, 1010
 thrombosis in, *Jan.*, 1010
 treatment, errors in, *Nov.*, 877
 valvular, in phthisis, *March*, 1527
 vital capacity of lungs in, *May*, 1655
 cases illustrating, *May*, 1664
 displacement of, in phthisis, *March*, 1524
 failure, advanced, anasarca in, relief, *July*, 130
 diet in, *July*, 129
 digitalis in, *July*, 132
 dyspnea in, treatment, *July*, 140
 edema in, relief, *July*, 131
 elimination in, *July*, 131
 general management, *July*, 124
 Karell diet in, *July*, 137
 management of bowels in, *July*, 131
 orthopnea in, treatment, *July*, 140
 ouabain in, *July*, 134, 135
 pain in, treatment, *July*, 140
 paracentesis in, *July*, 139
 promotion of diuresis in, *July*, 138
 relief of anasarca in, *July*, 137
 of edema in, *July*, 137
 respiratory symptoms, *July*, 140
 rest in, *July*, 124
 salt-free diet in, *July*, 138
 sleep in, *July*, 126
 strophanthin in, *July*, 134, 135
 symptomatic treatment, *July*, 137
 theobromin in, *July*, 138
 theocin in, *July*, 138
 theophyllin in, *July*, 138
 treatment of, *July*, 121
 symptomatic, *July*, 137
 use of drugs acting upon heart, *July*, 132
- functional activity, *March*, 1313
 Capacity, *Nov.*, 879
 in phthisis, *March*, 1519
 irritable, of soldiers, variability of blood-pressure in, *July*, 261, 262
 mitral shape, *Sept.*, 388
 murmurs, case illustrating, *March*, 1323
 pain over, *March*, 1500
 reserve power, *May*, 1657

- Heart, rheumatic infection, in childhood, *Sept.*, 616
 routine examination, *Jan.*, 1196
 size of, in phthisis, *March*, 1519
 use of drugs acting upon, in advanced heart failure, *July*, 132
- Heart-block, *Jan.*, 1217
- Heart-failure, advanced, after-treatment of, *July*, 142
 prophylaxis of, *July*, 141
- Hemichorea, *May*, 1866
- Hemolytic anemia, *May*, 1733
 icterus in early life, *Jan.*, 1137
- Hemophilia, retinal hemorrhage in, *Jan.*, 1100
- Hemorrhage, cerebral, as cause of cyanosis in newborn, *Sept.*, 597
 retinal hemorrhage in, *Jan.*, 1095
 in nephritis, relation to retinal hemorrhage, *Jan.*, 1095
 retinal, *Jan.*, 1091
 etiology of, *Jan.*, 1100
 in acute aplastic anemia, *Jan.*, 1098
 in arteriosclerosis, *Jan.*, 1095
 in hemophilia, *Jan.*, 1100
 in nephritis, *Jan.*, 1091, 1902
 in pernicious anemia, *Jan.*, 1097
 in purpura, *Jan.*, 1100
 in scurvy, *Jan.*, 1100
 in secondary aplastic anemia, *Jan.*, 1098
 relation of hemorrhage in nephritis to, *Jan.*, 1095
- Hemorrhagic diathesis due to nephritis, *Jan.*, 1096
 purpura in nephritis, *Jan.*, 1096
- Hereditary dyspituitarism, cases illustrating, *March*, 1476
 syphilis, treatment, *Nov.*, 895
- Hernia, diaphragmatic, *Jan.*, 1074
 diagnosis of, *Jan.*, 1074
- Herpes zoster in diabetes, *July*, 237
- Herxheimer reaction, *March*, 1304
- Heterophoria, influence of, on general health, *July*, 337
 prevalence of, *July*, 337
 symptom-complex of, *July*, 339
 treatment of, *July*, 340
- Hiccough, *Jan.*, 1073
- High position of diaphragm as result of adhesive pleuritis and pulmonary fibrosis, *Jan.*, 1060
 with lessened motility, *Jan.*, 1058
- History taking in diseases of stomach, *Sept.*, 488
- Hormonic signs of anterior lobe of hypophysis, *Nov.*, 779
 of endocrine amenorrhea, *Nov.*, 683
- Hormonic signs of posterior lobe of hypophysis, *Nov.*, 780
- Hospital, social worker in, function of, *Sept.*, 372
- Howell's theory of blood-clotting, *Jan.*, 1006
- Hunger, air-, *March*, 1582
- Hunger-pain in diseases of stomach, *Sept.*, 488
- Hyaline thrombosis, *Jan.*, 1007
- Hypalgesia, *Nov.*, 700
- Hyperacidity in diseases of stomach, *Sept.*, 488
- Hyperalgesia, *Nov.*, 700
- Hyperesthesia, *Nov.*, 700
- Hyperpiesis, *July*, 296
- Hyperplastic perihepatitis, chronic, *March*, 1333
- Hyperpnea, *March*, 1575
- Hyperpyrexia, *Nov.*, 751
- Hypertension and transient auricular fibrillation, *July*, 333
 essential, *July*, 21, 296
 primary, *July*, 27
 renal function tests in, cases illustrating, *Sept.*, 527-530
 treatment of, *July*, 257, 275
 variability of blood-pressure in, *July*, 257
 vascular, with angina pectoris and cerebral hemorrhage, *May*, 1767
- Hypertremesthesia, *Nov.*, 700
- Hyperthyroidism, basal metabolism in, *Jan.*, 1001; *March*, 1415
 beginning with gastric symptoms, cases illustrating, *March*, 1446-1454
 creatinuria in, *March*, 1401
 pain in, *March*, 1501
 variations in cases, from a clinical, laboratory, and therapeutic standpoint, *March*, 1393
- Hypertrophy, growth, *March*, 1598
- Hypesthesia, *Nov.*, 700
- Hypoesthesia, *Nov.*, 700
- Hypogenitalism, *Jan.*, 1143
- Hypoglycemia, critical period of, in undernutrition, *May*, 1728
- Hypophysis, anterior lobe, hormonal signs, *Nov.*, 779
 posterior lobe, hormonal signs, *Nov.*, 780
- Hypopincalism, *Jan.*, 1148
- Hypotension, variability of blood-pressure in, *July*, 257
- Hysterical fever, *Nov.*, 750
- Ice liver of Curschmann, *Nov.*, 849
- Lead liver, *March*, 1333

- Icterus, hemolytic, in early life, *Jan.*, 1137
- Idiopathic anemia, *Jan.*, 1239
- Ileopyloric reflex, *March*, 1588
- Iliac colon, spasm of, *Nov.*, 904
- Indican reaction in chronic intestinal indigestion from malassimilation of starch in children, *Sept.*, 627
- Indigestion, chronic intestinal, from starch showing indican reaction in children, *Sept.*, 621
- Infancy, disturbed weight in, *Nov.*, 889
- Infant feeding, lactic acid in, *Nov.*, 891
- Hercules, *March*, 1368
- Infantile diarrhea, *Nov.*, 737
- enteritis and, differentiation, *Nov.*, 737
- severe, *Nov.*, 717
- treatment of, *Nov.*, 722
- treatment, *Nov.*, 744
- Infections, fever in, *Nov.*, 747
- focal, and arthritis, *Nov.*, 655
- jaundice due to, *March*, 1305
- Inflammatory conditions, subdiaphragmatic, *May*, 1871
- Influenza, complications and sequels, management, *July*, 29
- thrombosis in, *Jan.*, 1009
- Influenzal pneumonia, serum and blood of convalescent patients in treatment of, *Jan.*, 937
- Intrapulmonary empyema, diagnosis, *July*, 91
- Insanity, manic-depressive, *Nov.*, 931
- Inspection of diaphragm, *Jan.*, 1049
- Intercostal nerve, neuritis of, pain of, *March*, 1500
- Interlobar pleural effusions, diagnosis of, *July*, 104
- Internal secretions, diseases of, problems in, *Jan.*, 1141
- secretory disturbance, gastric dysfunction in cases of, *Jan.*, 1227
- Intestinal indigestion, chronic, from starch showing indican reaction in children, *Sept.*, 621
- Intoxications, jaundice due to, *March*, 1305
- Intraspinal treatment of neurosyphilis, *Nov.*, 897
- tumor, epidural, case illustrating, *May*, 1799
- Irritable heart of soldiers, variability of blood-pressure in, *July*, 261, 262
- JAUNDICE, causes, *March*, 1304, 1305
- congenital, *March*, 1305
- due to infections and intoxications, *March*, 1305
- Jaundice following administration of arsphenamin, *March*, 1293
- cases illustrating, *March*, 1293-1303
- obstructive, *March*, 1305
- Joints, involvement of, in scarlatina, *March*, 1565
- KARELL diet in advanced heart failure, *July*, 137
- Ketosis, *July*, 352
- causes of, *July*, 352
- treatment of, *July*, 358
- Kidney, diabetic, *July*, 177
- function tests, *Sept.*, 513
- clinical application, *Sept.*, 513
- gouty, *Jan.*, 1043
- vascular supply, *May*, 1639
- Krauss's method of determining capillary pressure, *July*, 248
- LACTIC acid milk in infant feeding, *Nov.*, 891
- Legs, spontaneous thrombosis in, *Jan.*, 1014
- Lethargic encephalitis after influenza, *July*, 46
- Leukemia, acute monocytic, case illustrating, *March*, 1635
- atypical cases, 1607-1637
- basal metabolism in, *March*, 1412
- classification, *March*, 1607
- leukopenic, *March*, 1608
- lymphatic, chronic, case illustrating, *March*, 1629
- lymphoid, leukocytes of, *March*, 1612
- monocytic, *March*, 1613
- myeloid, leukocytes of, *March*, 1610
- Leukemic blood, oxidase reaction of cells in, *March*, 1614
- Leukocytes of lymphoid leukemia, *March*, 1612
- of myeloid leukemia, *March*, 1610
- of normal blood, *March*, 1609
- Leukopenic leukemia, *March*, 1608
- myeloma, case illustrating, *March*, 1615, 1620
- Leukosarcoma cells, *March*, 1613
- Leukosarcomatosis, Sternberg's, case illustrating, *March*, 1629
- Libman's drying-out treatment in blood transfusion, *March*, 1517
- Line, white adrenal, *Jan.*, 1230
- Litten's diaphragm sign, *Jan.*, 1049
- Liver, cirrhosis of, classification, *Sept.*, 555
- factors influencing production of symptoms in, *Sept.*, 557, 559

- Liver, cirrhosis of, of unknown etiology, *Sept.*, 564
 showing jaundice and ascites, *Sept.*, 555
 observations on frequency of symptoms and signs, *Sept.*, 561
 time of appearance, *Sept.*, 559
 ice, of Curschmann, *Nov.*, 849
 iced, *March*, 1333
 pericarditic pseudocirrhosis, *March*, 1333
- Lobar pneumonia, *Sept.*, 571
 age incidence, *Sept.*, 573
 bilateral, *Sept.*, 557
 complications, *Sept.*, 578
 concurrent diseases, *Sept.*, 579
 convalescence in, management, *March*, 1423
 double, *Sept.*, 575
 gross pathology, *Sept.*, 576
 lung involvement, *Sept.*, 574
 management of convalescence in, *March*, 1423
 pleural exudate in, *Sept.*, 577
 prevention, *July*, 191
 prophylactic vaccination against, *July*, 193
 serum and blood of convalescent patients in treatment of, *Jan.*, 937
 treatment, *July*, 191, 199
 method of administering serum, *July*, 201
 reaction to serum, *July*, 203
 serum sickness after, *July*, 204
 sex incidence, *Sept.*, 573
- Lumbago, *Jan.*, 973, 975
 acupuncture in, *Jan.*, 977
 chronic, *Jan.*, 977
- Lumbar puncture as routine procedure, *Jan.*, 1202
- Lungs, abscess of, localized pyopneumothorax and, differentiation, *July*, 98
 and diaphragm, effusions encapsulated between, diagnosis, *July*, 90
 and mediastinum, effusions encapsulated between, diagnosis, *July*, 92
 involvement of, in scarlatina, *March*, 1572
 malignant disease of, *May*, 1811
 diagnosis, *May*, 1828
 symptoms, *May*, 1827
 treatment, *May*, 1832
 massive collapse, diaphragm in, *Jan.*, 1062
- Lungs, routine examination, *Jan.*, 1198
 syphilis of, *May*, 1785
 diagnosis, *May*, 1796
 differential diagnosis, *May*, 1789
 frequency, *May*, 1792
 pathology, *May*, 1794
 prognosis, *May*, 1796
 symptoms, *May*, 1795
 treatment, *May*, 1797
 vital capacity, in heart disease, *May*, 1655
 cases illustrating, *May*, 1664
- Lutein, *Nov.*, 691
 ampules, *Nov.*, 691
- Lymphatic leukemia, chronic, case illustrating, *March*, 1629
- Lymphemia, *March*, 1608
- Lymph-nodes, enlarged, in neck, in scarlatina, *March*, 1563
- Lymphoid leukemia, leukocytes of, *March*, 1612
- MALIGNANT disease of lungs, *May*, 1811
 diagnosis, *May*, 1828
 symptoms, *May*, 1827
 treatment, *May*, 1832
- Manic-depressive insanity, *Nov.*, 931
- Marantic thrombi, *Jan.*, 1008
- Massive collapse of lung, diaphragm in, *Jan.*, 1062
- Mastoiditis complicating scarlatina, *March*, 1556
- Mediastinopericarditis, chronic, cardiolytic for, *Nov.*, 835
- Mediastinum and lung, effusions encapsulated between, diagnosis, *July*, 92
- Medical and social treatment, interrelation, *Sept.*, 371-382
- Medical-social clinic, *Sept.*, 371
- Mesenteric thrombosis, *Jan.*, 1012
- Metabolic rate, basal, in deficiency of adrenals, *Nov.*, 782
 of gonads, *Nov.*, 781
 in endocrine disturbance, *Nov.*, 775
 in pituitarism, *Nov.*, 777
 in pluriglandular syndromes, *Nov.*, 782
 in thyroidism, *Nov.*, 775
- Metabolism, basal, clinical value, *March*, 1403
 determination of, *March*, 1403
 limitations, in diagnosis, *March*, 1483
 with Benedict portable respiration apparatus, *March*, 1404

- Metabolism, basal, in diabetes mellitus, *March*, 1410
in disease, *March*, 1408
in diseases of thyroid gland, *March*, 1415
in heart disease, *March*, 1411
in hyperthyroidism, *Jan.*, 1001; *March*, 1415
in leukemia, *March*, 1412
in nephritis, *March*, 1411
in obesity, *March*, 1409
in pernicious anemia, *March*, 1412
in tuberculosis, *March*, 1414
in typhoid fever, *March*, 1413
value of, *Jan.*, 989
protein, in fevers, *Nov.*, 748
Migrating thrombosis, *Jan.*, 1014
Milk, lactic acid, in infant feeding, *Nov.*, 891
modified, preparation of, *Sept.*, 593
Milk-leg, *Jan.*, 1010
Mitral shape of heart, *Sept.*, 388
stenosis, auscultation in diagnosis, *Sept.*, 389
cases illustrating, *Sept.*, 401-416; *March*, 1315
classification, *Sept.*, 399
diagnosis, *Sept.*, 383
differential, *Sept.*, 395
electrocardiogram in diagnosis, *Sept.*, 395
exercise in diagnosis, *Sept.*, 389
history in diagnosis, *Sept.*, 386
inspection in diagnosis, *Sept.*, 387
murmurs of, explanation, *Sept.*, 384
palpation in diagnosis, *Sept.*, 387
percussion in diagnosis, *Sept.*, 388
pulse in diagnosis, *Sept.*, 388
x-ray in diagnosis, *Sept.*, 393
Mock angina, *March*, 1492
Modified milk, preparation of, *Sept.*, 593
Monocytic leukemia, *March*, 1613
acute, case illustrating, *March*, 1635
Morawitz's theory of blood-clotting, *Jan.*, 1005, 1006
Moritz and von Tabora's method of determining venous pressure, *July*, 244
Motor functions, perversions in, *Nov.*, 696
Multiple serositis, *March*, 1329
cases illustrating, *March*, 1329, 1338
etiology, *March*, 1335
pathogenesis, *March*, 1336
Murmur, Flint, *Jan.*, 1197
Graham Steell, in mitral stenosis, *Sept.*, 391, 392, 393, 398
Murmurs, heart, case illustrating, *March*, 1323
of mitral stenosis, explanation, *Sept.*, 384
Muscle sense, *Nov.*, 701
Myelemia, *March*, 1608
leukopenic, case illustrating, *March*, 1615, 1620
Myeloblasts, *March*, 1612
amitotic, *March*, 1613
Myelogene, *March*, 1611
Myeloid leukemia, leukocytes of, *March*, 1610
Myelosis, acute aleukemic, case illustrating, *March*, 1615, 1623
chronic aleukemic, case illustrating, *March*, 1620
Myocardial insufficiency, abdominal symptoms of, *July*, 289
Myocarditis, chronic, case illustrating, *March*, 1320
in phthisis, *March*, 1532
Myxedema, chronic nephrosis in association with, *July*, 167
symptoms of, *May*, 1748
treatment of, *May*, 1749
with anemia, *May*, 1733, 1743
NEPHRITIS, *July*, 1
acute, functional tests in, cases illustrating, *Sept.*, 518-522
basal metabolism in, *March*, 1411
chronic diffuse, *July*, 169
cases illustrating, *July*, 172-174
parenchymatous, *July*, 145
clinical types, *July*, 145
inflammatory type, *July*, 169
mixed type, *July*, 175
non-inflammatory type, *July*, 145
with hydrops, *July*, 171
with edema, functional tests in, cases illustrating, *Sept.*, 522-525
without edema, functional tests in, cases illustrating, *Sept.*, 525-527
classification of, *July*, 14
complicating scarlatina, *March*, 1569
hemorrhage in, relation to retinal hemorrhage, *Jan.*, 1095
hemorrhagic diathesis due to, *Jan.*, 1096
in association with diabetes, *July*, 177
observations on, *Jan.*, 1103
cases illustrating, *Jan.*, 1103-1110

- Nephritis, purpura hæmorrhagica in, *Jan.*, 1096
retinal hemorrhage in, *Jan.*, 1091, 1092
Vollhard and Fahr's classification, *July*, 15
- Nephrosis, *July*, 14
chronic, *July*, 145
cases illustrating, *July*, 147-167
in association with myxedema, *July*, 167
rôle of endocrine glands in pathogenesis of, *July*, 169
with superimposed diffuse nephritis, *July*, 175
- Nerve function, cranial, practical points about, *Nov.*, 707
mechanism of respiration, *Jan.*, 1048
- Nervous patients, routine examination, *Jan.*, 1194
symptoms in diseases of stomach, *Sept.*, 489
system, central, diseases of, in children, vomiting in, *Sept.*, 443
physical examination, *Nov.*, 695
relation of, to fever, *Nov.*, 750
- Neuralgic pains in diabetes, *July*, 234
- Neurasthenia, fever in, *Nov.*, 753
- Neuritis of an intercostal nerve, pain of, *March*, 1500
- Neurocirculatory asthenia, *Nov.*, 754; *March*, 1522
variability of blood-pressure in, *July*, 257
- Neurologic aspects of chorea, *May*, 1863
causes of diabetes mellitus, *July*, 225
treatment, *July*, 238
conditions due primarily to diabetes mellitus, *July*, 226
not due primarily to diabetes mellitus, *July*, 236
of doubtful origin in diabetes, *July*, 237
diagnosis, essentials in, *Nov.*, 695
examination of gait, *Nov.*, 702
of pupils, *Nov.*, 703
of reflexes, *Nov.*, 698
of special senses, *Nov.*, 698
practical points in testing sensation, *Nov.*, 699
reflexes in, *Nov.*, 698, 709
special senses in, *Nov.*, 698
treatment, *July*, 238
- effects of diabetes mellitus, *July*, 226
examination, routine, *Jan.*, 1201
- Neuronitis, cellular peripheral, *July*, 227
- Neuronitis, peripheral, *July*, 227
terminal peripheral, *July*, 227
truncular peripheral, *July*, 227
- Neuropsychic reactions associated with disturbances of ovarian function, *Nov.*, 757
- Neuroses, gastric, relation of thyroid-adrenal apparatus in, *March*, 1440
- Neurosis in asthenics, *March*, 1544
- Neurosyphilis, intraspinal treatment, *Nov.*, 897
- Newborn, cyanosis in, causes, *Sept.*, 596
- Nitrogenous substances, retention of, diuretics in, *May*, 1653
- Nocturnal enuresis, epileptic fits, and backwardness, with dyspituitary markings, case illustrating, *March*, 1479
relation of pituitary to, *March*, 1464
- OBESITY, basal metabolism in, *March*, 1409
- Obstructive jaundice, *March*, 1305
- Occupational therapy in heart disease, *Nov.*, 887
- Oppenheim reflex, *Nov.*, 713
- Orthopnea in advanced heart failure, treatment, *July*, 140
- Orthostatic albuminuria, diagnosis, *March*, 1599
etiology, *March*, 1596
prognosis, *March*, 1600
spinal brace in treatment, *March*, 1595, 1602
symptoms, *March*, 1598
treatment, *March*, 1600
- Osteitis deformans, *Nov.*, 829
differential diagnosis, *Nov.*, 833
etiology, *Nov.*, 832
pathology, *Nov.*, 833
prognosis, *Nov.*, 834
treatment, *Nov.*, 834
- Otitis media complicating scarlatina, *March*, 1556
- Ouabain in advanced heart failure, *July*, 134, 135
- Ovarian function, disturbances of, neuropsychic reactions associated with, *Nov.*, 737
residue, *Nov.*, 692
substance, *Nov.*, 691
- Oxidase reaction of cells in leukemic blood, *March*, 1614
- PAGET's disease of bones, *Nov.*, 829
differential diagnosis, *Nov.*, 833

- Paget's disease of bones, etiology, *Nov.*, 832
 pathology, *Nov.*, 833
 prognosis, *Nov.*, 834
 treatment, *Nov.*, 834
- Pain from overuse of tobacco, *March*, 1501
 in advanced heart failure, treatment, *July*, 140
 in aortic disease, *March*, 1499
 in disease of coronary arteries, *March*, 1498
 in hyperthyroidism, *March*, 1501
 in lower back, *Jan.*, 973
 treatment, *Jan.*, 987
 in neuritis of an intercostal nerve, *March*, 1500
 in pleurisy, *March*, 1500
 over heart, *March*, 1500
 referred, *Jan.*, 974
 from prostatic disease, *Jan.*, 984
- Palpation in diagnosis of mitral stenosis, *Sept.*, 387
 in examination of stomach, *Sept.*, 494
 of diaphragm, *Jan.*, 1050
- Paracentesis in advanced heart failure, *July*, 139
- Paralysis of diaphragm, *Jan.*, 1067
 spastic, in children, *Sept.*, 417
- Parenchymatous nephritis, chronic, *July*, 145
 clinical types, *July*, 145
 inflammatory type, *July*, 169
 mixed type, *July*, 175
 non-inflammatory type, *July*, 145
 with hydrops, *July*, 171
- Paresis, *Nov.*, 915
- Paresthesia, *Nov.*, 700
- Parietal effusions, diagnosis, *July*, 90
 encapsulated pleural effusions, diagnosis, *July*, 70
- Parotitis complicating typhus fever, *May*, 1890
- Paroxysmal auricular tachycardia, *May*, 1708, 1710
 tachycardia, *Nov.*, 909; *Jan.*, 1218, 1219
 treatment, *May*, 1710
- Pathologic reflexes, *Nov.*, 699
- Percussion in diagnosis of mitral stenosis, *Sept.*, 388
 in examination of stomach, *Sept.*, 495
 of diaphragm, *Jan.*, 1053
- Perennial asthma, *May*, 1751
- Pericardial effusion, low position of diaphragm from, *Jan.*, 1070
- Pericarditic pseudocirrhosis of liver, *March*, 1333
- Pericarditis, adhesive, chronic, etiology of, *Nov.*, 851
 operative treatment, *Nov.*, 852
 in phthisis, *March*, 1534
- Pericardium, adherent, *Nov.*, 835
 operative treatment, *Nov.*, 852
- Perihepatitis, chronic hyperplastic, *March*, 1333
- Peripheral neuronitis, *July*, 227
 cellular, *July*, 227
 thrombosis, *Jan.*, 1010
- Perivisceritis, *March*, 1333
- Pernicious anemia, *Jan.*, 1017, 1239
 basal metabolism in, *March*, 1412
 etiology, *Jan.*, 1240, 1241
 gastro-intestinal symptoms, *Jan.*, 1239
 in early life, *Jan.*, 1131
 treatment, *Jan.*, 1138
 of pregnancy, *May*, 1733
 prognosis, *Jan.*, 1252
 retinal hemorrhage in, *Jan.*, 1097
 spinal cord symptoms, *Jan.*, 1239
 symptoms, *Jan.*, 1239
 treatment, *Jan.*, 1024, 1253
- Perpetual arrhythmia, *May*, 1710
- Pfuhl's sign, *Jan.*, 1065
- Phlebitis, *Jan.*, 1005
 after prostatectomy, *Jan.*, 1011
 clinical causes, *Jan.*, 1008
- Phlegmasia alba dolens, *Jan.*, 1010
- Phleum pratense as cause of hay-fever, *May*, 1678
- Phrenic nerve, paralysis of, diaphragm in, *Jan.*, 1067
- Phthalein test, *Sept.*, 513
- Phthisis, congenital heart disease in, *March*, 1530
 displacement of heart in, *March*, 1524
 functional cardiovascular disorders in, *March*, 1521
 heart in, *March*, 1519
 myocarditis in, *March*, 1532
 pericarditis in, *March*, 1534
 right ventricle in, *March*, 1533
 size of heart in, *March*, 1519
 thyrogenic cardiovascular disorders in, *March*, 1523
 valvular heart disease in, *March*, 1527
- Physical examination of nervous system, *Nov.*, 695
- Physiologic reflexes, *Nov.*, 698
- Pick's disease, *Nov.*, 849; *March*, 1333
- Pineal gland, rôle of, in precocious sexual development, *Jan.*, 1148
- Pituitarism, basal metabolic rate in, *Nov.*, 777

- Pituitary gland, disorders of, classification, *Nov.*, 781
 relation of, to adolescent epilepsy and nocturnal enuresis, *March*, 1464
 signs, classification, *Nov.*, 777
 Pituitrope, *March*, 1465
 Pleural effusions, encapsulated, between lung and diaphragm, diagnosis, *July*, 90
 and mediastinum, diagnosis, *July*, 92
 diagnosis of, *July*, 69
 fluid and air in association with, *July*, 96
 interlobar, diagnosis of, *July*, 104
 parietal, diagnosis of, *July*, 70
 secondary changes in chest associated with, *July*, 117
 low position of diaphragm from, *Jan.*, 1068
 exudate in lobar pneumonia, *Sept.*, 577
 Pleurisy, acute diaphragmatic, *Jan.*, 1056
 pain in, *March*, 1500
 Pleuritis, adhesive, high position of diaphragm as result of, *Jan.*, 1060
 Pluriglandular syndromes, basal metabolic rate in, *Nov.*, 782
 Pneumococcus vaccine, *July*, 193
 Pneumonia, atypical case, *Sept.*, 531
 complicating scarlatina, *March*, 1572
 empyema complicating, *Sept.*, 471
 diagnosis, *Sept.*, 481
 condition of patient, *Sept.*, 482
 exploratory puncture, *Sept.*, 483
 physical signs, *Sept.*, 482
 x-rays, *Sept.*, 483
 frequency, *Sept.*, 481
 mortality, *Sept.*, 485
 treatment, *Sept.*, 483
 types, *Sept.*, 478
 influenzal, serum and blood of convalescent patients in treatment of, *Jan.*, 937
 lobar, *Sept.*, 571
 age incidence, *Sept.*, 573
 bilateral, *Sept.*, 575
 complications of, *Sept.*, 578
 concurrent diseases, *Sept.*, 579
 convalescence in, management, *March*, 1423
 double, *Sept.*, 575
 gross pathology, *Sept.*, 576
 Pneumonia, lobar, lung involvement, *Sept.*, 574
 management of convalescence in, *March*, 1423
 pleural exudate in, *Sept.*, 577
 prevention of, *July*, 191
 prophylactic vaccination against, *July*, 193
 serum and blood of convalescent patients in treatment of, *Jan.*, 937
 treatment, *July*, 191, 199
 method of administering serum, *July*, 201
 reaction to serum, *July*, 203
 serum sickness after, *July*, 204
 sex incidence, *Sept.*, 573
 streptococcus, serum treatment, *July*, 204
 thrombosis in, *Jan.*, 1009
Poa pratensis as cause of hay-fever, *May*, 1678
 Pollen asthma, *May*, 1753
 Polyneuritis, diabetic, *July*, 236, 237
 Polyorrhomenitis, *March*, 1333
 Polyserositis, *March*, 1333
 Portal thrombosis, *Jan.*, 1011, 1012
 Postmeningitic dementia, *Nov.*, 919
 Postoperative thrombosis, *Jan.*, 1011
 Postural reflex, *Sept.*, 431
 Posture sense, *Nov.*, 701
 Precocious sexual development, *Jan.*, 1147, 1148
 rôle of pineal gland in, *Jan.*, 1148
 Pregnancy, circulatory disturbances, *July*, 179
 pernicious anemia of, *May*, 1733
 Presclerotic stage of atherosclerosis, *July*, 296
 Prophylactic vaccination against pneumonia, *July*, 193
 Prostatectomy, phlebitis after, *Jan.*, 1011
 Prostatic disease, referred pain from, *Jan.*, 984
 Protein metabolism in fevers, *Nov.*, 748
 Prothrombin, *Jan.*, 1006
 Pseudocirrhosis of liver, pericarditic, *March*, 1333
 Pseudoleukemic anemia in early life, *Jan.*, 1132
 cause, *Jan.*, 1133
 symptoms, *Jan.*, 1134
 treatment, *Jan.*, 1138
 Pseudoparesis alcoholica, *Jan.*, 1290
 Pseudotabes, diabetes, *July*, 231
 Psychosis, manic-depressive, *Nov.*, 931

- Puberty and climacterium, *July*, 59
 Puerperal thrombosis, *Jan.*, 1010
 Pulmonary complications in carcinoma of esophagus, *Jan.*, 1265
 fibrosis, high position of diaphragm as result of, *Jan.*, 1060
 infections, non-tuberculous, sub-acute and chronic, *Nov.*, 819
 blood changes in, *Nov.*, 824
 cough in, *Nov.*, 821
 onset of, *Nov.*, 820
 physical signs, *Nov.*, 822
 sputum in, *Nov.*, 825
 tuberculin tests in, *Nov.*, 826
 x-ray findings in, *Nov.*, 823
 thrombosis in heart disease, *Jan.*, 1010
 tuberculosis, heart in, 1519. See also *Phthisis*.
 Pulse in diagnosis of mitral stenosis, *Sept.*, 388
 Pulsus alternans, *Jan.*, 1222
 Puncture, lumbar, as routine procedure, *Jan.*, 1202
 Pupils, practical points about, *Nov.*, 703
 Purpura hæmorrhagica in nephritis, *Jan.*, 1096
 retinal hemorrhage in, *Jan.*, 1100
 Pus infections of rectosigmoid regions, *Nov.*, 906
 Pylephlebitis, *Jan.*, 1012
 Pyloric stenosis in children, vomiting in, *Sept.*, 439
 Pylorospasm in children, vomiting in, *Sept.*, 439
 Pyopneumothorax, localized, abscess of lung and, differentiation, *July*, 98
 subdiaphragmatic, *Jan.*, 1066
 RACHITIC splenomegaly, *Jan.*, 1133
 Ragweed, dwarf, as cause of hay-fever, *May*, 1679
 Rapid heart action, *May*, 1707
 cases illustrating, *May*, 1712-1721
 Rash in scarlatina, *March*, 1554, 1555
 Reaction, Herxheimer, *March*, 1304
 Rectal contractures, *Nov.*, 904
 Rectosigmoid angle, *Nov.*, 901
 atony of, *Nov.*, 907
 region, pus infections of, *Nov.*, 906
 spastic contracture, *Nov.*, 904
 Rectum, routine examination, *Jan.*, 1024
 Referred pain, *Jan.*, 974
 from prostatic disease, *Jan.*, 984
 Reflex, abdominal, *Nov.*, 714
 Babinski, *Nov.*, 713
 Chaddock, *Nov.*, 713, 714
 cremasteric, *Nov.*, 714
 Gordon, *Nov.*, 713
 ileopyloric, *March*, 1588
 Oppenheim, *Nov.*, 713
 postural, *Sept.*, 431
 sole, *Nov.*, 714
 vomiting in children, *Sept.*, 444
 Reflexes in diabetes mellitus, *July*, 226
 in neurologic diagnosis, *Nov.*, 698, 709
 pathologic, *Nov.*, 699
 physiologic, *Nov.*, 698
 Rehfuess test for examination of stomach contents, *Sept.*, 498
 Renal function, *May*, 1639
 as measured by elimination of fluids, salt and nitrogen, and specific gravity of urine, *July*, 209
 test-meal for, *July*, 209
 tests, *Sept.*, 513
 clinical application, *Sept.*, 513
 two-hour test for, *July*, 209
 glycosuria, *March*, 1375, 1388;
 May, 1731
 sclerosis, 16
 Reserve power of heart, *May*, 1657
 Residual blood-pressure, *July*, 259
 Respiration, abnormal, *March*, 1575
 nerve mechanism, *Jan.*, 1048
 Respiratory quotient, *Jan.*, 991
 non-protein, *Jan.*, 992
 symptoms in advanced heart failure, *July*, 140
 Rest in advanced heart failure, *July*, 124
 Retinal hemorrhage, *Jan.*, 1091
 etiology, *Jan.*, 1100
 in acute aplastic anemia, *Jan.*, 1098
 in arteriosclerosis, *Jan.*, 1095
 in cerebral hemorrhage, *Jan.*, 1095
 in hemophilia, *Jan.*, 1100
 in nephritis, *Jan.*, 1091, 1092
 in pernicious anemia, *Jan.*, 1097
 in purpura, *Jan.*, 1100
 in scurvy, *Jan.*, 1100
 in secondary aplastic anemia, *Jan.*, 1098
 relation of hemorrhage in nephritis to, *Jan.*, 1095
 Reversible secondary sex phenomena, *March*, 1345
 cases illustrating, *March*, 1346-1372

- Rheumatic fever, acute, *March*, 1326
infection of heart in childhood, *Sept.*, 616
Rickettsia prowazeki, *May*, 1879, 1880
Roman wormwood as cause of hay-fever, *May*, 1679
Romberg's sign, *Nov.*, 701
Routine procedures in clinical medicine, *Jan.*, 1173
Rule, Gibson, *Jan.*, 1005
Rumination in children, *Sept.*, 444
- SACRO-ILIAC joint disease, *Jan.*, 982
Salt and nitrogen content of urine, amount, *Sept.*, 517
Salt-free diet in advanced heart failure, *July*, 138
Scarlatina, *March*, 1553
arthritis complicating, *March*, 1566, 1568
convalescent blood in, *March*, 1559
desquamation in, *March*, 1557, 1558
enlarged lymph-nodes in neck complicating, *March*, 1563
etiology, *March*, 1553
involvement of joints in, *March*, 1565
of lungs in, *March*, 1572
mastoiditis complicating, *March*, 1556
nephritis complicating, *March*, 1569
otitis media complicating, *March*, 1556
pneumonia complicating, *March*, 1572
rash in, *March*, 1554, 1555
septic type, *March*, 1559, 1562
stage of shrinking, *March*, 1556
of swelling, *March*, 1554
treatment, *March*, 1574
Zingher's treatment, *March*, 1559
Scarlet fever, *March*, 1553. See also *Scarlatina*.
Sclerosis, renal, *July*, 16
Scurvy, retinal hemorrhage in, *Jan.*, 1100
Seasonal hay-fever, causes, *May*, 1673
treatment, *May*, 1673
Secondary sex phenomena, reversive, *March*, 1345
cases illustrating, *March*, 1346-1372
Secretions, internal, diseases of, problems in, *Jan.*, 1141
Sensation, dissociation of, *Nov.*, 701
practical points in testing, *Nov.*, 699
Sense, muscle, *Nov.*, 701
Senses, special, in neurologic diagnosis, *Nov.*, 698
- Sepsis as cause of cyanosis in newborn, *Sept.*, 597
Septic type of scarlatina, *March*, 1559, 1562
Sergent white line, *Jan.*, 1230
Serositis, multiple, *March*, 1329
cases illustrating, *March*, 1329, 1338
etiology of, *March*, 1335
pathogenesis of, *March*, 1336
Serum, antipneumococcus, in lobar pneumonia, *July*, 191
in streptococcus pneumonia, *July*, 204
of convalescent patients in treatment of lobar and influenzal pneumonia, *Jan.*, 937
sickness after serum treatment of pneumonia, *July*, 204
treatment of lobar pneumonia, *July*, 191, 199
method of administering serum, *July*, 201
reaction to serum, *July*, 203
serum sickness after, *July*, 204
of streptococcus pneumonia, *July*, 204
Sex phenomena, reversive secondary, *March*, 1345
cases illustrating, *March*, 1346-1372
Sexual development, precocious, *Jan.*, 1148
rôle of pineal gland in, *Jan.*, 1148
organs, routine examination, *Jan.*, 1201
Sickness, serum, after serum treatment of pneumonia, *July*, 204
Sigmoidospasm, *Nov.*, 904
Sign, Broadbent's, *Nov.*, 852
diaphragm, of Litten, *Jan.*, 1049
Fürbringer's, *Jan.*, 1065
Pfuhl's, *Jan.*, 1065
Romberg's, *Nov.*, 701
Williams', *Jan.*, 1078
Sinus arrhythmia, *Jan.*, 1219
Size and weight in boarding-school boys, *May*, 1899
Sleep in advanced heart failure, *July*, 126
Sleeping sickness, *Sept.*, 543
after influenza, *July*, 46
Social and medical treatment, interrelation, *Sept.*, 371-382
worker, *Sept.*, 371
in hospital, function of, *Sept.*, 372
Sodium chlorid retention, diuretics in, *May*, 1652

- Sole reflex, *Nov.*, 714
- Spasm, low position of diaphragm from, *Jan.*, 1073
- of diaphragm, *Jan.*, 1073
- of iliac colon, *Nov.*, 904
- sphincter, *Nov.*, 904
- Spastic contracture of rectosigmoid region, *Nov.*, 904
- paralysis in children, *Sept.*, 417
- Specific gravity of urine, fixation, two-hour test for, *Sept.*, 514
- Sphincter spasm, *Nov.*, 904
- Spinal brace in treatment of orthostatic albuminuria, *March*, 1595, 1602
- Spine, tumor of, differential diagnosis, case illustrating, *May*, 1799
- Splenic thrombosis, *Jan.*, 1011
- Splenomegaly, primary, with anemia, in early life, *Jan.*, 1136
- rachitic, *Jan.*, 1133
- Spondylitis, *Jan.*, 980
- Spontaneous thrombosis in legs, *Jan.*, 1014
- Spring tonometer for measuring capillary pressure, *July*, 250
- Sputum bacteria, relation of, to asthma, *May*, 1758
- in subacute and chronic non-tuberculous pulmonary infections, *Nov.*, 825
- Status thymicolymphaticus, *Jan.*, 1257
- thymicus, *Jan.*, 1022
- Stenosis, mitral, auscultation in diagnosis, *Sept.*, 389
- cases illustrating, *Sept.*, 401-416; *March*, 1315
- classification of, *Sept.*, 399
- diagnosis of, *Sept.*, 383
- differential, *Sept.*, 395
- electrocardiogram in diagnosis, *Sept.*, 395
- exercise in diagnosis, *Sept.*, 389
- Graham Steell murmur in, *Sept.*, 391, 392, 393, 398
- history in diagnosis, *Sept.*, 386
- inspection in diagnosis, *Sept.*, 387
- murmurs of, explanation, *Sept.*, 384
- palpation in diagnosis, *Sept.*, 387
- percussion in diagnosis, *Sept.*, 388
- pulse in diagnosis, *Sept.*, 388
- x-ray in diagnosis, *Sept.*, 395
- pyloric, in children, vomiting in, *Sept.*, 439
- Sternberg's leukosarcomatosis, case illustrating, *March*, 1629
- Stomach, cancer of, diagnosis, *Sept.*, 492, 510
- Stomach, cancer of, x-rays in diagnosis, *Sept.*, 510
- contents, examination of, *Sept.*, 495
- emptying time of, *Sept.*, 505
- examination of, blood tests, *Sept.*, 500
- cancer, *Sept.*, 492
- contents, *Sept.*, 495
- history taking, *Sept.*, 488
- hunger-pains, *Sept.*, 488
- hyperacidity, *Sept.*, 488
- modern, *Sept.*, 487
- nervous symptoms, *Sept.*, 489
- palpation, *Sept.*, 494
- percussion, *Sept.*, 495
- physical examination of patient, *Sept.*, 494
- re-examinations and follow-up system, *Sept.*, 503
- Rehfuess test, *Sept.*, 498
- stomach-tube, *Sept.*, 497
- string test, *Sept.*, 500
- test breakfast, *Sept.*, 497
- of capacity, *Sept.*, 495
- x-rays, *Sept.*, 501
- modern examination, *Sept.*, 487
- normal definition of, *Sept.*, 504
- ulcer of, anatomic results of treatment, *Sept.*, 509
- chronic, diagnosis of, *Sept.*, 506
- Stomach-tube in examination of stomach, *Sept.*, 497
- Streptococcus pneumonia, serum treatment, *July*, 204
- String test for examination of stomach, *Sept.*, 500
- Strophanthin in advanced heart failure, *July*, 134, 135
- Stuttering, bladder, *Sept.*, 640
- Subcostal angle, costal margins, movement of, *Jan.*, 1050
- Subdiaphragmatic abscess, *Jan.*, 1063, 1065
- elevation of diaphragm in, *Jan.*, 1063
- inflammatory conditions, *May*, 1871
- pyopneumothorax, *Jan.*, 1066
- Subfebrile fever, *Nov.*, 751
- Submaxillary glands, infection of, complicating typhus fever, *May*, 1890
- Subnormal fever, *Nov.*, 751
- Summer diarrhea, *Nov.*, 737
- Supplemental breast feeding, *Nov.*, 734
- Swift-Ellis method of intraspinal therapy in syphilis, *Nov.*, 897
- Syndrome, effort, *Nov.*, 754
- Fröhlich's, with epileptic fits and nocturnal enuresis, case illustrating, *March*, 1472
- genito-adrenal, *March*, 1367

- Vomiting in pyloric stenosis in children, *Sept.*, 439
 in pylorospasm in children, *Sept.*, 439
 persistent, in children, *Sept.*, 443
 reflex, in children, *Sept.*, 444
 with high fever in children, *Sept.*, 440
 von Jaksch's disease, *Jan.*, 1132
 von Tabora and Moritz's method of determining blood-pressure, *July*, 244
- WACHSTUMSHYPERTROPHIE, *March*, 1598
 Weight and size in boarding-school boys, *May*, 1899
 disturbed, in infancy, *Nov.*, 889
 Weil-Felix reaction in typhus fever, *May*, 1892
 White adrenal line, *Jan.*, 1230
 Wilbur and Addis' method of estimating urobilin and urobilinogen, *July*, 287
- Williams' sign, *Jan.*, 1078
 Wormwood, Roman, as cause of hay-fever, *May*, 1679
- x-RAY findings in subacute and chronic non-tuberculous pulmonary infections, *Nov.*, 823
 x-Rays in diagnosis, *Jan.*, 1205
 of cancer of stomach, *Sept.*, 510
 of empyema complicating pneumonia, *Sept.*, 483
 of mitral stenosis, *Sept.*, 395
 in examination of diaphragm, *Jan.*, 1054
 of stomach, *Sept.*, 501
 in treatment of malignant disease of lungs, *May*, 1832
- ZENKER'S degeneration in influenza, *July*, 52
 Zingher's treatment in scarlet fever, *March*, 1559
 Zuckergussleber, *March*, 1333

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CONTENTS OF VOLUME 4

July, 1920

NEW YORK NUMBER

Clinic of Dr. Nellis B. Foster, <i>Cornell Division, New York Hospital</i> NEPHRITIS.....	PAGE 1
Clinic of Dr. Harlow Brooks, <i>University and Bellevue Hospital Medical College</i> THE COMPLICATIONS AND SEQUELAE OF INFLUENZA AND THEIR MANAGEMENT.....	29
Clinic of Dr. S. W. Bandler, <i>Post-Graduate Hospital</i> PUBERTY AND CLIMACTERIUM. A STUDY IN ENDOCRINES.....	59
Clinic of Dr. H. Wessler, <i>Mt. Sinai Hospital</i> THE DIAGNOSIS OF ENCAPSULATED PLEURAL EFFUSIONS.....	69
Clinic of Dr. Cary Eggleston, <i>From the Department of Pharmacology, Cornell University Medical College, and the Second Medical (Cornell) Division of Bellevue Hospital</i> THE TREATMENT OF ADVANCED HEART FAILURE.....	121
Clinic of Dr. Albert A. Epstein, <i>Mt. Sinai Hospital</i> CLINICAL TYPES OF CHRONIC PARENCHYMATOUS NEPHRITIS—THEIR TREATMENT AND RESULTS.....	145
Clinic of Dr. W. W. Herrick, <i>Roosevelt Hospital</i> SOME PHASES OF THE CIRCULATORY DISTURBANCES OF PREGNANCY: WITH AN ILLUSTRATIVE CASE.....	179
Clinic of Dr. Russell L. Cecil, <i>Bellevue Hospital (Second Medical Division)</i> THE PREVENTION AND SERUM TREATMENT OF LOBAR PNEUMONIA.....	191
Clinic of Dr. Herman O. Mosenthal, <i>Department of Metabolism, Vanderbilt Clinic</i> RENAL FUNCTION AS MEASURED BY THE ELIMINATION OF FLUIDS, SALT AND NITROGEN, AND THE SPECIFIC GRAVITY OF THE URINE. THE APPLICATION OF THE METHOD TO AMBULANT PATIENTS.....	209
Clinic of Dr. Walter M. Kraus, <i>Department of Metabolism, Vanderbilt Clinic</i> THE NEUROLOGIC CAUSES AND EFFECTS OF DIABETES MELLITUS AND THEIR TREATMENT..	225
Clinic of Dr. Henry Elsner Marks, <i>Department of Metabolism, Vanderbilt Clinic</i> THE CLINICAL DETERMINATION OF VENOUS AND CAPILLARY PRESSURES.....	239
Clinic of Dr. Ernst P. Boas, <i>Department of Metabolism, Vanderbilt Clinic</i> THE INTERPRETATION OF HIGH BLOOD-PRESSURE READINGS.....	257
Clinic of Dr. Louis Bauman, <i>Presbyterian Hospital</i> TWO CASES ILLUSTRATING THE CLINICAL SIGNIFICANCE OF UROBILIN. SUMMARY OF OUR PRESENT KNOWLEDGE OF THE SUBJECT.....	251
Contribution by Dr. Burrill B. Crohn EARLY ABDOMINAL SYMPTOMS OF MYOCARDIAL INSUFFICIENCY.....	289
Clinic of Dr. S. J. Nilson, <i>St. Bartholomew's Clinic</i> DIET IN ECZEMA.....	301

Clinic of Dr. S. Neuhof, Lebanon Hospital and Central and Neurological Hospital	PAGE
AURICULAR FIBRILLATION.....	307
Clinic of Dr. Walter F. Macklin, New York Throat, Nose, and Lung Hospital	
THE PREVALENCE OF HETEROPHORIA AND ITS INFLUENCE UPON GENERAL HEALTH.....	337
Clinic of Dr. Max Kahn, Beth Israel Hospital	
CLINICAL SIGNIFICANCE OF ACIDOSIS.....	345
Clinic of Dr. M. B. Rosenblüth, Fordham University Medical School	
GLANDULAR FEVER.....	361

September, 1920

BOSTON NUMBER

Contribution by Ida M. Cannon, Chief of Social Service Department, Massachusetts General Hospital	PAGE
A MEDICAL-SOCIAL CLINIC.....	371
Contribution by Drs. Paul D. White and William D. Reid, From the Cardiac Clinic of the Massachusetts General Hospital	
THE DIAGNOSIS OF MITRAL STENOSIS.....	383
Clinic of Dr. Stanley Cobb, Massachusetts General Hospital	
SPASTIC PARALYSIS IN CHILDREN.....	417
Clinic of Dr. Maynard Ladd, Children's Department, Boston Dispensary	
VOMITING AS A SYMPTOM IN CHILDREN.....	437
Clinic of Dr. Edward H. Nichols, Boston City Hospital	
SUGGESTIONS REGARDING THE EARLY DIAGNOSIS OF ACUTE APPENDICITIS.....	449
Clinic of Dr. William H. Robey, Jr., Boston City Hospital	
ANEURYSM OF THE DESCENDING AORTA.....	459
Clinic of Dr. Edwin A. Locke, Pneumonia Service, Boston City Hospital	
EMPHYEMA COMPLICATING PNEUMONIA.....	471
Clinic of Dr. Franklin W. White, Boston City Hospital	
THE MODERN EXAMINATION OF THE STOMACH.....	487
Clinic of Dr. W. Richard Ohler, Boston City Hospital	
RENAL FUNCTION TESTS—THEIR CLINICAL APPLICATION.....	513
Clinic of Dr. M. J. English, Boston City Hospital (From the Clinic of Dr. William H. Robey, Jr.)	
AN ATYPICAL CASE OF PNEUMONIA.....	531
Clinic of Dr. Albert A. Hornor, Boston City Hospital	
ENCEPHALITIS.....	543
Clinic of Dr. H. Archibald Nissen, Boston City Hospital	
CIRRHOSIS OF THE LIVER SHOWING JAUNDICE AND ASCITES. AN ANALYTIC STUDY OF 117 CASES.....	555
Contribution by Dr. Frank B. Berry (From the Pathological Laboratory of Boston City Hospital)	
LOBAR PNEUMONIA. ANALYSIS OF 400 AUTOPSIES.....	571
Clinic of Dr. John Lovett Morse, Children's Hospital	
CONSTIPATION AND ECZEMA IN AN INFANT FROM AN EXCESS OF FAT IN MODIFIED MILK	585
Clinic of Dr. Lewis Webb Hill, Children's Hospital	
1. CONGENITAL ATELECTASIS. 2. BRONCHIAL TETANY.....	595
Clinic of Dr. Edwin T. Wyman, Children's Hospital	
TWO CASES OF ACQUIRED HEART DISEASE IN CHILDHOOD.....	607

	PAGE
Clinic of Dr. Karlton G. Percy, <i>Children's Hospital</i> CHRONIC INTESTINAL INDIGESTION FROM STARCH SHOWING INDICAN REACTION. REPORT OF 33 CASES.....	621
Clinic of Dr. Joseph I. Grover, <i>Children's Hospital</i> ENTRESIS.....	631
Clinic of Dr. Phillip H. Sylvester, <i>Children's Hospital</i> A CASE FOR DIAGNOSIS.....	643
<hr/>	
November, 1920	ST. LOUIS NUMBER
Clinic of Dr. George Dock, <i>Barnes' Hospital</i> FOCAL INFECTION AND ARTHRITIS.....	655
Clinic of Dr. William Engelbach, <i>St. John's Hospital</i> ENDOCRINE AMENORRHEA.....	665
Clinic of Dr. William Washington Graves, <i>St. Louis City Hospital</i> THE PHYSICAL EXAMINATION OF THE NERVOUS SYSTEM OR SOME OF THE ESSENTIALS IN NEUROLOGIC DIAGNOSIS.....	695
Clinic of Dr. W. McKim Marriott, <i>St. Louis Children's Hospital</i> SEVERE DIARRHEA IN INFANCY.....	717
Clinic of Dr. Borden S. Veeder (<i>Clinic on Normal Feeding at Municipal Welfare Con- ference</i>), <i>Washington University Medical School</i> COMPLEMENTAL BREAST FEEDING.....	729
Clinic of Dr. John Zahorsky, <i>St. Louis City Hospital</i> TWO CASES OF INFANTILE DIARRHEA.....	737
Clinic of Dr. Charles Hugh Nellson, <i>Department of Medicine, St. Louis University School of Medicine</i> FEVER IN GENERAL, WITH SPECIAL REFERENCE TO SLIGHT ELEVATIONS OF TEMPERATURE AND THEIR CLINICAL SIGNIFICANCE.....	747
Clinic of Dr. Francis M. Barnes, Jr., <i>From the Department of Nervous and Mental Diseases, St. Louis University</i> SOME NEUROPSYCHIC REACTIONS ASSOCIATED WITH DISTURBANCES OF OVARIAN FUNCTION..	757
Clinic of Dr. John L. Tierney, <i>St. John's Hospital</i> THE BASAL METABOLIC RATE IN ENDOCRINE DISTURBANCE.....	775
Clinic of Dr. Ralph A. Kinsella, <i>Medical Clinic, St. Mary's Hospital, St. Louis Uni- versity School of Medicine</i> ENDOCARDITIS.....	813
Clinic of Dr. J. Curtis Lyter, <i>St. Anthony's Hospital</i> THE SUBACUTE AND CHRONIC NON-TUBERCULOUS PULMONARY INFECTIONS.	819
Clinic of Dr. Louis Henry Hempelmann, <i>Evangelical Deaconess Hospital</i> PACET'S DISEASE OF THE BONES (OSTEITIS DEFORMANS).....	829
Clinic of Dr. Ellsworth S. Smith, <i>Barnes' Hospital</i> CARDIOLYSIS FOR CHRONIC MEDIASTINOPERICARDITIS, WITH REPORT OF 2 CASES AND REVIEW OF LITERATURE TO DATE	835
Contribution by Dr. W. H. Olmsted, <i>Department of Internal Medicine, Washington University School of Medicine, Metabolism Laboratories</i> THE USE OF 5 PER CENT VEGETABLES IN THE TREATMENT OF DIABETES MELLITUS	865
Clinic of Dr. Drew Luten, <i>Barnes' Hospital</i> ERRORS IN THE DIAGNOSIS AND TREATMENT OF HEART DISEASE... ..	877
Clinic of Dr. Jules M. Brady, <i>St. Ann's Hospital</i> DISTURBED WEIGHT IN INFANCY	889

6 CONTENTS OF VOLUME 4

Clinic of Dr. P. C. Jeans, <i>St. Louis Children's Hospital</i> TREATMENT OF HEREDITARY SYPHILIS.....	PAGE 895
Clinic of Dr. Horace W. Soper CLINICAL TYPES OF CHRONIC CONSTIPATION.....	901
Clinic of Dr. Llewellyn Sale, <i>St. Louis City Hospital</i> PRESENTATION OF A CASE OF PAROKYSMAL TACHYCARDIA.....	909
Clinic of Dr. Sidney I. Schwab, <i>Barnes' Hospital</i> FIVE CASES FROM THE NEUROLOGIC CLINIC OF BARNES' HOSPITAL	913
<hr/>	
<i>January, 1921</i>	PHILADELPHIA NUMBER
Clinic of Dr. Alfred Stengel, <i>University Hospital</i> ON THE USE OF SERUM AND BLOOD OF CONVALESCENT PATIENTS IN THE TREATMENT OF LOBAR PNEUMONIA AND INFLUENZAL PNEUMONIA.....	PAGE 937
Clinic of Dr. Thomas McGrae, <i>Jefferson Hospital</i> PAIN IN THE LOWER BACK.....	973
Contribution by Drs. M. Howard Fussell and Leon Jonas, <i>University of Pennsylvania</i> CALORIMETRY: ITS APPLICATION IN CLINICAL MEDICINE.....	989
Clinic of Dr. David Riesman, <i>Philadelphia General Hospital</i> PHLEBITIS AND THROMBOSIS.....	1005
Clinic of Dr. Joseph Saller, <i>Philadelphia General Hospital</i> A CASE OF PERNICIOUS ANEMIA.....	1017
Clinic of Dr. George William Norris, <i>Pennsylvania Hospital</i> TOPHACEOUS GOUT.....	1029
Clinic of Dr. Elmer H. Funk, <i>Jefferson Hospital</i> THE DIAPHRAGM: ANATOMIC AND PHYSIOLOGIC CONSIDERATIONS; METHODS OF EXAMINATION; CONDITIONS ASSOCIATED WITH ALTERED POSITION OF THE DIAPHRAGM; DIAPHRAGMATITIS.....	1045
Clinic of Dr. Henry R. M. Landis, <i>University Hospital</i> ANEURYSM OF THE THORACIC AORTA.....	1083
Clinic of Dr. O. H. Perry Pepper, <i>University Hospital</i> MEDICAL ASPECTS OF RETINAL HEMORRHAGE.....	1091
Clinic of Dr. John H. Musser, Jr., <i>Fram the Nephritic Clinic of the Medical Dispensary, University Hospital</i> OBSERVATIONS ON NEPHRITIS.....	1103
Clinic of Dr. John H. Musser, Jr., <i>Presbyterian Hospital</i> SOME UNUSUAL MANIFESTATIONS OF CEREBROSPINAL SYPHILIS.....	1111
Clinic of Dr. J. P. Crozer Griffith, <i>University Hospital</i> TYPES OF ANEMIA AS SEEN IN EARLY LIFE.....	1125
Clinic of Dr. Francis X. Dercum, <i>Jefferson Hospital</i> PROBLEMS IN DISEASES OF THE INTERNAL SECRETIONS, WITH ILLUSTRATIVE CASES....	1141
Clinic of Dr. B. B. Vincent Lyon, Assisted by Drs. Henry J. Bartle, Richard T. Ellison, and Russell Richardson, <i>Jefferson Hospital</i> A DISCUSSION OF THE TREATMENT OF A CASE OF CHRONIC ARTHRITIS, WITH LAMBLIASIS, BY DUODENAL BILIARY DRAINAGE.....	1153
Clinic of Dr. Edward J. G. Beardsley, <i>Jefferson Hospital</i> THE NECESSITY FOR AND THE IMPORTANCE OF ROUTINE PROCEDURES IN CLINICAL MEDICINE.	1173

Clinic of Dr. Charles C. Woffert, <i>From the Cardiovascular Clinic, Medical Out-Patient Department, University Hospital</i>	PAGE
ABNORMAL CARDIAC RHYTHMS AND THEIR DIFFERENTIATION BY SIMPLE METHODS.....	1207
Clinic of Dr. Truman G. Schnabel, <i>From the Gastro-intestinal Clinic, Medical Out-Patient Department, University Hospital</i>	
GASTRIC DYSFUNCTION IN CASES OF INTERNAL SECRETORY DISTURBANCE.....	1227
Clinic of Dr. Henry K. Mohler, <i>Jefferson Hospital</i>	
PERNICIOUS ANEMIA—GASTRO-INTESTINAL AND SPINAL CORD SYMPTOMS. REPORT OF A CASE.....	1239
ADDISON'S DISEASE—DISCUSSION OF SYMPTOMS. REPORT OF A CASE WITH AUTOPSY FINDINGS.....	1255
Clinic of Dr. T. Grier Miller, <i>University Hospital</i>	
CARCINOMA OF THE ESOPHAGUS.....	1265
Clinic of Dr. Joseph C. Doane, <i>Philadelphia General Hospital</i>	
SOME MANIFESTATIONS OF ALCOHOLISM.....	1283
<hr/>	
<i>March, 1921</i>	NEW YORK NUMBER
Clinic of Dr. Warfield T. Longcope, <i>Presbyterian Hospital</i>	PAGE
JAUNDICE FOLLOWING THE ADMINISTRATION OF AEPHENAMIN.....	1293
Clinic of Dr. T. Stuart Hart, <i>Presbyterian Hospital</i>	
THE FUNCTIONAL ACTIVITY OF THE HEART, METHOD OF CLASSIFICATION.....	1313
Clinic of Dr. Albert R. Lamb, <i>Presbyterian Hospital</i>	
MULTIPLE SEROSITIS.....	1329
Contribution by Dr. George Draper, <i>Presbyterian Hospital</i>	
REVERSIVE SECONDARY SEX PHENOMENA.....	1345
Clinic of Dr. H. Rawle Geyelin, <i>Presbyterian Hospital</i>	
THE SIGNIFICANCE OF GLYCOSURIA.....	1375
Clinic of Drs. Bertram J. Sanger and Louis Bauman, <i>Presbyterian Hospital</i>	
VARIATION IN CASES OF HYPERTHYROIDISM FROM A CLINICAL, LABORATORY, AND THERAPEUTIC STANDPOINT.....	1395
Contribution by Drs. Herman O. Mosenthal and Henry E. Marks, <i>Post-Graduate Hospital</i>	
THE CLINICAL VALUE OF BASAL METABOLISM.....	1403
Clinic of Dr. Harlow Brooks, <i>The University and Bellevue Medical College</i>	
MANAGEMENT OF CONVALESCENCE IN LOBAR PNEUMONIA.....	1423
Clinic of Dr. A. S. Blumgarten, <i>Lenox Hill Hospital</i>	
THE RÔLE OF THE ENDOCRINES IN COMMON MEDICAL DISEASES.....	1437
Contribution by Dr. William S. McCann, <i>From the Russell Sage Institute of Pathology in Affiliation with the Second Medical Division (Cornell), Bellevue Hospital, New York</i>	
THE LIMITATIONS OF METABOLISM DETERMINATIONS IN DIAGNOSIS.....	1463
Clinic of Dr. Harold E. B. Pardee, <i>New York Hospital</i>	
DISEASE OF THE CORONARY ARTERIES.....	1491
Clinic of Dr. Reuben Ottenberg, <i>Mt. Sinai Hospital</i>	
PRACTICAL ASPECTS OF BLOOD TRANSFUSION.....	1509
Clinic of Dr. Ernst P. Boas, <i>Montefiore Home and Hospital</i>	
THE HEART IN THE TUBERCULOUS.....	1519
Clinic of Dr. John L. Kantor, <i>Department of Gastro-enterology, Vanderbilt Clinic, Columbia University</i>	
THE GENERAL MANAGEMENT OF FUNCTIONAL DIGESTIVE DISORDERS.....	1537
Clinic of Dr. Jesse G. M. Bullowa, <i>Willard Parker Hospital</i>	
SCARLATINA.....	1553

Clinic of Dr. David Preswick Barr, <i>From the Russell Sage Institute of Pathology, in Affiliation with the Second (Cornell) Medical Division of Bellevue Hospital, New York</i>	PAGE
DYSPNEA AND HYPERPNEA.....	1575
Clinic of Dr. Arthur L. Holland, <i>New York Hospital</i>	
THE SIGNIFICANCE OF SOME GASTRO-INTESTINAL SYMPTOMS.....	1585
Clinic of Dr. Murray H. Bass, <i>Mount Sinai Hospital</i>	
ORTHOSTATIC ALBUMINURIA, WITH SPECIAL REFERENCES TO ITS TREATMENT BY A SPINAL BRACE.....	1595
Clinic of Dr. N. Rosenthal, <i>Mount Sinai Hospital</i>	
SOME ATYPICAL CASES OF LEUKEMIA.....	1607

May, 1921

BOSTON NUMBER

Clinic of Dr. Henry A. Christian, <i>Peter Bent Brigham Hospital</i>	PAGE
RIGHT AND WRONG USE OF DIURETICS.....	1639
Clinic of Dr. Francis W. Peabody, <i>Peter Bent Brigham Hospital</i>	
THE VITAL CAPACITY OF THE LUNGS IN HEART DISEASE.....	165
Clinic of Dr. I. Chandler Walker, <i>Peter Bent Brigham Hospital</i>	
THE CAUSES AND TREATMENT OF SEASONAL HAY-FEVER.....	1673
Contribution by Dr. C. W. McClure, <i>Peter Bent Brigham Hospital</i>	
TREATMENT OF FUNCTIONAL GASTRO-INTESTINAL DISTURBANCES.....	1693
Clinic of Dr. Samuel A. Levine, <i>Peter Bent Brigham Hospital</i>	
RAPID HEART ACTION.....	1707
Clinic of Dr. Elliott P. Joslin, <i>New England Deaconess Hospital</i>	
PRACTICAL LESSONS FOR PHYSICIANS AND PATIENTS IN DIABETES.....	1723
Clinic of Dr. George R. Minot, <i>Massachusetts General Hospital</i>	
TWO CURABLE CASES OF ANEMIA.....	1733
Clinic of Dr. Francis M. Rackemann, <i>Massachusetts General Hospital</i>	
THE VACCINE TREATMENT OF ASTHMA.....	1751
Clinic of Dr. James P. O'Hare, <i>Peter Bent Brigham Hospital</i>	
A CASE OF VASCULAR HYPERTENSION WITH ANGINA PECTORIS AND CEREBRAL HEMORRHAGE. AUTOPSY.....	1767
Clinic of Dr. Edwin A. Locke, <i>Boston City Hospital</i>	
SYPHILIS OF THE LUNGS.....	1785
Contribution by Dr. Frederick T. Lord, <i>Massachusetts General Hospital</i>	
A DISCUSSION OF THE DIFFERENTIAL DIAGNOSIS OF A CASE OF SPINAL TUMOR	1799
Clinic of Dr. William H. Robey, <i>Boston City Hospital</i>	
MALIGNANT DISEASE OF THE LUNGS.....	1811
Clinic of Drs. Paul D. White and C. Sidney Burwell, <i>Massachusetts General Hospital</i>	
THE CLINICAL SIGNIFICANCE OF CHANGES IN THE FORM OF THE ELECTROCARDIOGRAM ..	1839
Clinic of Dr. Stanley Cobb, <i>Massachusetts General Hospital</i>	
SOME NEUROLOGIC ASPECTS OF CHOREA.....	1863
Clinic of Dr. Roger I. Lee, <i>Massachusetts General Hospital</i>	
SUBDIAPHRAGMATIC INFLAMMATORY CONDITIONS.....	1871
Contribution by Drs. Francis W. Palfrey and S. Burt Wolbach, <i>Harvard University Medical School</i>	
TYPHUS FEVER.....	1877
Contribution by Dr. Horace Gray, <i>New England Deaconess Hospital</i>	
SIZE AND WEIGHT IN 130 BOARDING-SCHOOL BOYS (MIDDLESEX)....	1899
Index of Columns	1915



